McKnight Brain Research Foundation
New Trustee
Orientation Materials

July 2023

McKnight Brain Research Foundation
New Trustee Orientation Materials
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Public Website: https://mcknightbrain.org
Website Management: BRG Communications
Contact person: Valerie Patmintra
Private Secure Website: https://tmbrf.org/board-login/
Website Management: Beck Digital
Contact Person: Melanie Cianciotto

Evelyn Franks McKnight

Founder and Benefactor of the McKnight Brain Research Foundation

November 10, 1914 – October 2, 1999

…A brief biography

Evelyn Franks McKnight, daughter of Arthur and Bertha Franks of Connellsville, Pennsylvania, blazed a trail of recognition and accomplishments throughout her life from November 10, 1914, to October 2, 1999. Following high school, she studied to become a nurse. Evelyn's mother, a seamstress, supplied the financial support for her daughter's nursing education. After leaving Connellsville, she launched her career as a registered nurse. For six years prior to Evelyn's emigration to Florida in 1946, she was employed in the Congress of the United States as a licensed nurse in the District of Colombia. During the Korean War she worked as a Captain in the United States Air Force at the Pentagon.

After her retirement from the Air Force, Evelyn returned to Miami, Florida, where she worked in the personnel section of the Trans World Airlines (TWA), followed by her employment as a staff nurse at the Miami Veterans Administration Medical Center (VAMC). Evelyn retired from the VAMC in 1965 and joined the registry for private duty nursing. She met William L. McKnight when she worked as his nurse. They were married in 1974 after the death of his first wife in 1973.

William McKnight was with the 3M Company for 59 years prior to his retirement in 1966 as President and Chairman of the Board. A multimillionaire industrialist and philanthropist, Mr. McKnight owned a large home on La Gorce Island, Miami Beach, Florida, and had many business interests in the Miami-Dade County area. He owned the Hialeah Park for horse racing and was chairman of the board of Miami's Calder Race Course and Tropical Park. Mr. McKnight also owned the popular and upscale Tony Sweet's Restaurant. He was a founding member and chairman of the board of the Surf Club, a very prestigious social club on Miami Beach, Florida.

The McKnights, together, were very interested in the philanthropic causes he had pursued through his previously established McKnight Foundation. These focused primarily on human services related to physical and social problems, grants for health and medical research, education plus the visual and performing arts. The McKnights' interest in the nervous system and the relationship between the eye and brain inspired their gift to the Bascom Palmer Eye Institute at the University of Miami to establish the William. L. McKnight Vision Research Center. They are among the largest contributors to the Bascom Palmer Eye Institute and the University of Miami.

During their marriage, William and Evelyn McKnight were favorite guests at many social functions. Often, upon leaving a social gathering, William would say to Evelyn…"Why is it I can't remember that person's name until after I've just left them?" As a result, and with Evelyn's background as a nurse, they became very interested in supporting research in memory loss related to the aging process. Prior to William's death in 1978, he and Evelyn would drive around Dade County on Sunday afternoons looking for property to build a brain institute to support research in cognitive decline and memory loss associated with the aging process.

Over the two decades after Mr. McKnight's death, Evelyn quietly oversaw and remained interested in and dedicated to maintaining the legacy of Mr. McKnight in both his business and philanthropic interests. As a result, on April 28, 1999, she established the McKnight Brain Research Foundation to support research of the brain to accomplish alleviation of memory loss of the aging as a legacy to her deceased husband.

Before Mrs. McKnight could realize the value of her gift in advancing the understanding and alleviation of age-related memory loss, she died on October 2, 1999. She will always be remembered as a gracious and gentle lady who accomplished great things and made a difference in the lives of many.

McKnight Brain Research Foundation (MBRF)

Vision, Value Statement, and Mission

Vision:

To: "Improve the quality of life through the understanding and alleviation of age-related memory loss."

Value Statement:

- ***Commitment***

  The MBRF is committed to its vision to understand and alleviate age-related memory loss, and expects the same of its grant recipients and research partners.

- ***Discovery***

  The MBRF values scientific curiosity and discovery leading to clinical intervention in age-related memory loss.

- ***Honesty/Integrity***

  The MBRF conducts its affairs with the highest degree of honesty, integrity, and accountability and expects the same of others.

Mission:

Lead in generating interest and support of scientific research to understand and alleviate age-related memory loss.

Inspire commitment and shared vision in the understanding and alleviation of age-related memory loss.

Nurture scientists dedicated to the exploration of innovative research initiatives intended for clinical application in age-related memory loss.

Promote collaboration and communication among research scientists, institutions, and organizations engaged in research in age-related memory loss.

Partner with research scientists, institutions, and organizations to promote research to understand and alleviate age-related memory loss.

Recognize and Reward significant achievement in discoveries leading to clinical intervention to understand and alleviate age-related memory loss.

Vision, Value Statement, Mission Adopted May 18, 2005
Reaffirmed July 22, 2020

McKnight Brain Research Foundation

Strategic Plan

McKnight Brain Research Foundation Vision Statement:

To:

"Improve the quality of life through the understanding and alleviation of age related memory loss."

Approved October 18, 2006
Reaffirmed November 1, 2012
Reaffirmed October 14, 2014
Reaffirmed February 6, 2017

McKnight Brain Research Foundation Value Statement:

- *Commitment*
  - *The MBRF is committed to its vision to understand and alleviate age-related memory loss, and expects the same of its grant recipients and research partners*

- *Discovery*
  - *The MBRF values scientific curiosity and discovery leading to clinical intervention in age related memory loss*

- *Honesty/Integrity*
  - *The McKnight Brain Research Foundation (MBRF) conducts its affairs with the highest degree of honesty, integrity, and accountability and expects the same of others*

Approved October 18, 2006
Reaffirmed November 1, 2012
Reaffirmed February 6, 2017

McKnight Brain Research Foundation Mission Statement

•***Lead*** *in generating interest and support of scientific research to understand and alleviate age-related memory loss**

•***Inspire*** *commitment and shared vision in the understanding and alleviation of age-related memory loss*

•***Nurture*** *scientists dedicated to the exploration of innovative research initiatives intended for clinical application in age-related memory loss*

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•***Partner*** *with research scientists, institutions, and organizations to promote research to understand and alleviate age-related memory loss*

•***Recognize and Reward*** *significant achievement in discoveries leading to clinical intervention to understand and alleviate age-related memory loss*

Approved December 11, 2006
Reaffirmed November 1, 2012
Amended October 14, 2014
Amended February 6, 2017

** The specific influence of aging on memory loss*

Mission, Goal, Strategy Planning

Mission Statement	Goal	Strategies
• Lead in generating interest and support of scientific research to understand and alleviate age-related memory loss	• Increase the number of institutions, researchers, organizations and scientists whose focus is to understand and alleviate age-related memory loss • Explore new avenues of potential research within the scientific community which could lead to the development of therapeutic and behavioral interventions and, ultimately, to improved outcomes for age related memory loss • Raise the level of awareness both within the scientific community and among the public about the importance of research in age related memory loss and its tremendous value to society	• Grant/Gift agreements • FNIH/NIA/MBRF Summit • Public outreach communications plan-Tactics-Website, media, communications • Seminars, symposia, colloquia • Inter-Institutional Meeting • Leadership Council • Travel Award Program • IOM Study • Assess the status of the current scientific knowledge in the normal aging and changes in cognition associated with the aging process • Identify research scientists whose research focus is compatible with the MBRF vision • Citations in publications and presentations • Research Partnership (NIA) • Inter-disciplinary cores • Develop an annual operating plan and budget • Consider communications as a partnership approach for future discussions

Mission, Goal, Strategy Planning

Mission Statement	Goal	Strategies
• Lead in generating interest and support of scientific research to understand and alleviate age-related memory loss	• Identify cross-disciplinary research emphasizing practical approaches to the development of therapeutic and lifestyle interventions designed to facilitate cognitive trajectories in the aging population • Assure the progress towards the vision and goals of the Foundation is achieved • Influence the content of curricula for undergraduate, postgraduate medical education • Influence the requirements for both initial and maintenance of board certification and professional licensure	• Grant/Gift agreements • FNIH/NIA/MBRF Summit • Develop a Communications Plan – tactics, Website, media, communications • Seminars, symposia, colloquia • Inter-Institutional Meeting • Leadership Council • Travel Award Program • IOM Study • Assess the status of the current scientific knowledge in the normal aging and changes in cognition associated with the aging process • Identify research scientists whose research focus is compatible with the MBRF vision • Citations in publications and presentations • Research Partnerships (NIA) • Inter-disciplinary cores • Educate and advocate curricula standards with examining boards and accrediting bodies • Educate and advocate with professional testing, licensing and accrediting authorities

Mission, Goal, Strategy Planning

Mission Statement	Goal	Strategies
• Inspire commitment and shared vision in the understanding and alleviation of age related memory loss	• Educate and raise the level of awareness in the scientific community about the importance of research in age-related memory loss and its tremendous value to society • Encourage the increase in the number of institutions, scientists, researchers, organizations that share the vision • Foster an environment that would enhance the interest and focus on the recruitment of highly talented individuals into the field • Educate and raise the level of awareness among the public about the importance of research in age related memory loss, the impact on their lifestyle and families. • Attract and cultivate partners to leverage awareness, education and funding of age-related memory loss.	• Grant/Gift agreements • Increase the number of graduate and post-doctoral students in the field • MBRF hosted Society for Neuroscience Poster Session • Develop a Communications plan – tactics, Website, media, communications • Seminars, symposia, colloquia, etc. • Targeted awards, for both new investigators and students • National spokesperson • IOM study • NIA Partnership • Targeted outreach to potential partners (public and private foundations, etc.) • Conversation with grantee institutions Memory Intervention Core to leverage strategies • Endowed Chairs • Lectureship

Mission, Goal, Strategy Planning

Mission Statement	Goal	Strategies
• Promote collaboration and communication among research scientists, institutions, and organizations engaged in research in age-related memory loss	• Increase collective understanding and knowledge of the process of learning and age-related memory loss • Sharing of the information and research in age-related memory loss • Accelerate discoveries leading to the understanding and alleviation of age related memory loss • Increase awareness of current research within the scientific community for age related memory loss	• Requirements in Grant/Gift agreements to collaborate • FNIH/NIA/MBRF Summit • Website, media, communications • Scientific Publications • Seminars, symposia, colloquia • Inter-Institutional Meeting • Leadership Council • Focus groups • Travel Award Program • IOM Study • MBRF hosted Society for Neuroscience Poster Session • Site visits • Recognition and rewards • Establishing Brain Institutes committed to the vision of MBRF • Research Partnerships • Shared database of list of projects, scientists, etc. with brief description, contact person info • CME offerings • Block grants

Mission, Goal, Strategy Planning

Mission Statement	Goal	Strategies
• Nurture scientists dedicated to exploration and innovative research initiatives intended for clinical application in age-related memory loss	• Encourage and support scientists whose main focus is to understand and alleviate age-related memory loss • Foster innovation • Expand the number of research scientists whose focus is to understand and alleviate age-related memory loss • Facilitate development of therapeutic interventions for age-related memory loss	• Ensuring that the institution fosters an environment conducive to the success of the research scientist • Seed grants directed toward innovation • New investigator awards • Travel Award Program • Track all post-doctoral fellows and/or trainees in programs or institutions that have received MBRF funding • Increase the number of graduate and post-doctoral fellows and/or trainees in the field • MBRF hosted Society for Neuroscience Poster Session • Clinical research fellowship awards either alone or in partnership with other funding individuals or organizations

Mission, Goal, Strategy Planning

Mission Statement	Goal	Strategies
• Partner with research scientists, institutions, and organizations to promote research to understand and alleviate age-related memory loss	• Leverage the financial and intellectual resources of the Foundation • Raise the level of awareness of the understanding and alleviation of age-related memory loss • Promote cooperation and collaboration within the scientific community • Through partnerships, explore new avenues of potential research within the scientific community which could lead to the development of therapeutic, behavioral and life style interventions to improve outcomes for the aging population • Attract and cultivate partners to leverage awareness, education and funding of age-related memory loss.	• FNIH/NIA/MBRF Summit • Seminars, symposia, colloquia • Establish McKnight Brain Institutes • Grant/Gift agreements • Research Partnership with NIA and FNIH • Partner with other national organizations • Match funding with MBRF • Targeted outreach to potential partners • Consider communications as a partnership approach for future discussions • Inter-Institutional Meetings

Mission, Goal, Strategy Planning

Mission Statement	Goal	Strategies
• Recognize and Reward significant achievement in discoveries leading to clinical intervention to understand and alleviate age-related memory loss	• Provide Incentive and encouragement • Increase awareness • Focus the outcome on clinical applications • Expand the number of research scientists whose focus is to understand and alleviate age-related memory loss • Reward and retain existing talent within the field • Recognize scientific achievements in age related memory loss	• Research prize awards • Young investigator awards • Seed grants • New investigator awards • Develop relationships with other institutions and organizations to increase awareness • Individual communication • Public Communication • MBRF hosted Society for Neuroscience Poster Session • Clinical research fellowship awards either alone or in partnership with other funders or organizations

Guidelines for funding

- Receptivity
- Amount of investment by MBRF, duration and ability to leverage matching funds
- Reputation
- Impact
- Innovation
- Opportunity for synergy
- Monitoring requirements
- Potential for success
- Physical and human resources (facilities and manpower)
- Honesty, integrity and commitment to transparency and accountability

Approved November 1, 2012
Amended October 14, 2014
Amended February 6, 2017

McKnight Brain Research Foundation Mission Statement

- ***Lead*** *in generating interest and support of scientific research to understand and alleviate age-related memory loss**

- ***Inspire*** *commitment and shared vision in the understanding and alleviation of age-related memory loss*

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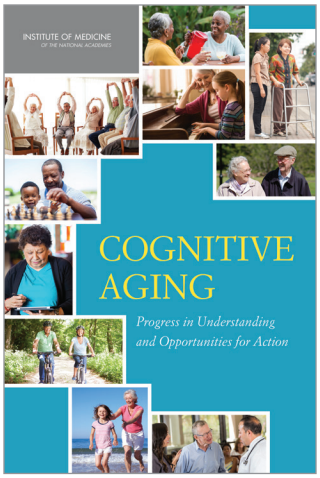
Cognitive Aging

Progress in Understanding and Opportunities for Action



For most Americans, staying "mentally sharp" as they age is a very high priority. Declines in memory and decision-making abilities may trigger fears of Alzheimer's disease or other neurodegenerative diseases. However, cognitive aging is a natural process that can have both positive and negative effects on cognitive function in older adults—effects that vary widely among individuals. At this point in time, when the older population is rapidly growing in the United States and across the globe, it is important to examine what is known about cognitive aging and to identify and promote actions that individuals, organizations, communities, and society can take to help older adults maintain and improve their cognitive health.

With support from the McKnight Brain Research Foundation, the National Institute on Aging, the National Institute of Neurological Disorders and Stroke, AARP, the Retirement Research Foundation, and the Centers for Disease Control and Prevention, the Institute of Medicine (IOM) convened a committee to examine the public health dimensions of cognitive aging. In *Cognitive Aging: Progress in Understanding and Opportunities for Action*, the committee assesses the state of knowledge about cognitive aging, including definitions and terminology, epidemiology and surveillance, prevention and intervention, education of health professionals, and public awareness and education.

It is important to identify and promote actions that individuals, organizations, communities, and society can take to help older adults maintain and improve their cognitive health.

What Is Cognitive Aging?

Like other organs, the human brain changes with age in both its physical structures and its ability to carry out various functions. The brain is responsible for cognition, a term that includes memory, decision making, processing speed, wisdom, and learning. As a person ages, these functions may change—a process called cognitive aging.

Cognitive aging is not a disease. Instead, it is a process that occurs in every individual, beginning at birth and continuing throughout the life span.

Cognitive changes are different for each person, and an individual's cognitive function may vary from one day to another. Wisdom and expertise can increase with age, while speed of processing, decision making, and some types of memory may decline. Cognitive aging may affect daily tasks such as paying bills, driving, following recipes, and adhering to medication schedules. It may challenge an older person's ability to live independently, pursue favorite activities, and maintain a sense of identity. But there are specific actions that individuals and their families can take to support their cognitive function. It is important to overcome stigma and misconceptions that may prevent older adults from seeking resources that can promote their cognitive health and overall quality of life.

Steps for Individuals to Reduce Risks for Cognitive Decline

Despite wide variation in cognitive function among individuals, the committee identifies three actions, supported by scientific evidence, that everyone can take to maintain their cognitive health and potentially reduce the effects of cognitive aging. Specifically, the committee recommends that individuals should

1. Be physically active.
2. Reduce and manage cardiovascular disease risk factors (including hypertension, diabetes, and smoking).
3. Regularly discuss and review health conditions and medications that might influence cognitive health with a health care professional.

The committee also identifies additional actions for which there is some scientific evidence to suggest positive effects on cognitive health:

- Be socially and intellectually engaged, and continually seek opportunities to learn.

Characterizing Cognitive Aging

Key Features

- Inherent in humans and animals as they age.
- Occurs across the spectrum of individuals as they age regardless of initial cognitive function.
- Highly dynamic process with variability within and between individuals.
- Includes some cognitive domains that may not change, may decline, or may actually improve with aging, and there is the potential for older adults to strengthen some cognitive abilities.
- Only now beginning to be understood biologically yet clearly involves structural and functional brain changes.
- Not a clinically-defined neurological or psychiatric disease such as Alzheimer's disease and does not inevitably lead to neuronal death and neurodegenerative dementia (such as Alzheimer's disease).

Risk and Protective Factors

- Health and environmental factors over the life span influence cognitive aging.
- Modifiable and non-modifiable factors include genetics, culture, education, medical comorbidities, acute illness, physical activity, and other health behaviors.
- Cognitive aging can be influenced by development beginning in utero, infancy, and childhood.

Assessment

- Cognitive aging is not easily defined by clear thresholds on cognitive tests since many factors—including culture, occupation, education, environmental context, and health variables (e.g., medications, delirium)—influence test performance and norms.
- For an individual, cognitive performance is best asessed at several points in time.

Impact on Daily Life

- Day-to-day functions, such as driving, making financial and health care decisions, and understanding instructions given by health care professionals, may be affected.
- Experience, expertise, and environmental support aids (e.g., lists) can help compensate for declines in cognition.
- The challenges of cognitive aging may be more apparent in environments that require individuals to engage in highly technical and fast-paced or timed tasks, situations that involve new learning, or stressful situations (i.e., emotional, physical, or health-related), and less apparent in highly familiar situations.

It is important to overcome stigma and misconceptions that may prevent older adults from seeking resources that can promote cognitive health and overall quality of life.

- Get adequate sleep and receive treatment for sleep disorders as needed.
- Take steps to avoid the risks of cognitive changes due to delirium if hospitalized.

Finally, individuals and families should be aware of the potential for financial fraud and abuse, impaired driving skills, and poor consumer decision making, and they should make health, finance, and consumer decisions based on reliable evidence from trusted sources.

Steps for Health Care Providers to Address Cognitive Aging

Individuals and families are turning to health care professionals in increasing numbers for information and advice about cognitive health. These professionals need to be fully informed and ready to respond to patient queries. However, although cognitive aging occurs in every individual (compared with about 11 to 14 percent of older Americans who experience Alzheimer's disease or other dementias), there is relatively little research or clinical guidance about risk and protective factors or interventions for non-disease age-related declines in cognition. As a result, many health care providers consider cognitive health counseling a challenge.

The committee recommends that health professional schools, professional societies, and public and private health care organizations develop and disseminate core competencies, curricula, and continuing education opportunities that focus on cognitive aging (as distinct from clinical syndromes and diseases). Furthermore, the committee stresses that cognitive health should be promoted during regular medical and wellness visits for people of all ages. Specifically, health care professionals should use patient visits to

- identify risk factors for cognitive decline and recommend steps to minimize risk;
- review patient medications, especially those known to affect cognition;
- provide patients and families with information about cognitive aging and actions that may maintain cognitive health or prevent decline; and
- encourage patients and family members to discuss concerns about cognitive health.

Community Support, Policy Change, and Private-Sector Business Involvement to Address Cognitive Aging

The effects of cognitive aging have widespread societal consequences and require action in many sectors. An array of public health and social services are available to assist older adults and their families, and communities across the country are working to improve quality of life for aging individuals, but many challenges remain. Opportunities for action include

- Collect and disseminate population-based data on cognitive aging.
- Develop an independent information gateway on cognitive aging as well as consumer-relevant criteria for evaluating cognition-related products.
- Involve the financial, transportation, and technology industries in developing and implementing products, services, and informational materials focused on (1) maintaining and assessing older adults' driving skills

and making family decisions about safe driving; (2) banking and financial decision vulnerabilities; and (3) technology opportunities to accommodate cognitive changes.

Public Education and Engagement

Promoting cognitive health for older adults requires clear and effective communication with the public. Messages should be accurate, up-to-date, and consistent; resonate with diverse groups within the U.S. population; and encourage behaviors that promote cognitive health. Differentiating cognitive aging from Alzheimer's disease and dementia will be a major challenge for public information campaigns. Although Alzheimer's disease and other neurodegenerative diseases are an important area of focus, the committee calls for more attention to the needs of the vast majority of the aging population whose change in cognitive function is not related to disease.

Conclusion

"Cognitive aging is not just an individual or a family or a health care system challenge," the committee writes, "it is an issue that affects the fabric of society and requires actions by many and varied stakeholders." *Cognitive Aging: Progress in Understanding and Opportunities for Action* offers clear steps that individuals, families, communities, health care providers and systems, financial organizations, community groups, public health agencies and others can take to promote cognitive health and help older adults live fuller and more independent lives. Ultimately, the report calls for a societal commitment to cognitive aging as a public health issue that requires prompt action across many sectors.

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Recommendations from Institute of Medicine Study on Cognitive Aging Release date, April 14
…Progress in Understanding and Opportunities for Action

Release date, April 14, 2015

Recommendation 1: ***Increase Research and Tools for Assessing Cognitive Aging and Cognitive Trajectories***

The National Institutes of Health, the Centers for Disease Control and Prevention, research foundations, academic research institutions, and private-sector companies should expand research on the trajectories of cognitive aging and improve the tools used to assess cognitive changes and their effects on daily function.

Specific needs include

- Studies using a range of assessments (e.g., neuronal injury biomarkers, neuroimaging, postmortem assessments of neuronal integrity) to explore the physiological and structural basis of cognitive aging;
- Non-human animal studies that examine the mechanisms and clinical correlates of cognitive aging and that are designed to inform human cognitive aging;
- Studies to examine the mechanisms underlying interventions that affect the cognitive trajectory;
- Studies to identify and validate novel tools and measures of function that capture the complexities of real-world tasks and are sensitive to early changes in cognition and function; and
- An update of the norms for cognitive function in older adults (including those in the most advanced age groups) to include the consideration of disease, literacy, language, racial and ethnic diversity , culture, and socioeconomic factors.

Recommendation 2: ***Collect and Disseminate Population-Based Data on Cognitive Aging***
The Centers for Disease Control and Prevention (CDC), state health agencies, and other relevant government agencies, as well as nonprofit organizations, research foundations, and academic research institutions, should strengthen efforts to collect and disseminate population-based data on cognitive aging. These efforts should identify the nature and extent of cognitive aging throughout the population, including high-risk and underserved populations, with the goal of informing the general public and improving relevant policies, programs and services.

Specifically, expanded cognitive aging data collection and dissemination efforts should include

- A focus on the cognitive health of older adults as separate from dementia or other clinical neurodegenerative diseases.
- The development of operational definitions of cognitive aging for use in research and public health surveillance and also the development of a process for periodic reexamination. Analyses of existing longitudinal datasets of older persons should be used to inform these efforts.
- Expanded data collection efforts and further analyses of representative surveys involving geographically diverse and high-risk populations. These efforts should include cognitive testing when standardized, feasible, and clinically credible and also self-reports of perceptions or concerns regarding cognitive aging, personal and social adaptations, and self-care and other management practices.
- Longitudinal assessments of changes in cognitive performance and risk behaviors in diverse populations.
- Inclusion of cognition-related questions in the core instrument of the Behavioral Risk Factor Surveillance System, rather than an optional module.
- Exploration of other available relevant data on cognitive health such as health insurance claims data, sales and marketing data for cognition-related products and treatments, data on financial and banking transactions as well as on financial fraud and scams, and data on automobile insurance claims.
- Active dissemination of data on cognitive aging in the population. An annual or biennial report to the U.S. public should be issued by the CDC or other federal agency on the nature and extent of cognitive aging in the U.S. population.

Recommendation 3: ***Take Actions to Reduce Risks of Cognitive Decline with Aging***
Individuals of all ages and their families should take actions to maintain and sustain their cognitive health, realizing that there is wide variability in cognitive health among individuals.

Specifically, individuals should:

- Be physically active.
- Reduce and manage cardiovascular disease risk factors (including hypertension, diabetes, smoking).
- Regularly discuss and review health conditions and medications that might influence cognitive health with a health care professional.
- Take additional actions that may promote cognitive health, including
  - Be socially and intellectually engaged, and engage in lifelong learning;
  - Get adequate sleep and receive treatment for sleep disorders if needed;
  - Take steps to avoid the risk of cognitive changes due to delirium if hospitalized; and
  - Carefully evaluate products advertised to consumers to improve cognitive health, such as medications, nutritionals, and cognitive training.

Recommendation 4: ***Increase Research on Risk and Protective Factors and Interventions to Promote Cognitive Health and Prevent or Reduce Cognitive Decline***
The National Institutes of Health, the Centers for Disease Control and Prevention, other relevant government agencies, nonprofit organizations, and research foundations should expand research on risk and protective factors for cognitive aging and on interventions aimed at preventing or reducing cognitive decline and maintaining cognitive health.

Research efforts should:

- Develop collaborative approaches between ongoing longitudinal studies across the life span that focus on cognitive aging outcomes in order to maximize the amount and comparability of data available on risk and protective factors.
- Examine risk factors and interventions in under-studied and vulnerable populations, including people 85 years and older and those with childhood or youth trauma or developmental
- delay, mental illness, learning disabilities, or genetic intellectual disabilities and spanning ethnic/cultural and socioeconomic groups.
- Conduct single- and multicomponent clinical trials of promising interventions to promote cognitive health and prevent cognitive decline, testing for both cognitive status and functional outcomes.
- Assess cognitive outcomes in clinical trials that target the reduction of cardiovascular and other risk factors likely related to cognitive health.
- Explore older adults' preferences and values regarding cognitive health and aging and regarding specific cognitive interventions and training modalities.
- Identify effective approaches to sustaining behavior changes that promote healthy cognition across the life span.

Recommendation 5: ***Ensure Appropriate Review, Policies, and Guidelines for Products That Affect Cognitive Function or Assert Claims Regarding Cognitive Health***

The Food and Drug Administration and the Federal Trade Commission, in conjunction with other relevant federal agencies and consumer organizations, should determine the appropriate regulatory review, policies, and guidelines for

- **over-the-counter medications (such as antihistamines, sedatives, and other medications that have strong anticholinergic activity) that may affect cognitive function, and**
- **interventions (such as cognitive training, nutriceuticals, supplements, or medications) that do not target a disease but may assert claims about cognitive enhancement or maintaining cognitive abilities such as memory or attention.**

Recommendation 6: ***Develop and Implement Core Competencies and Curricula in Cognitive Aging for Health Professionals***

The Department of Health and Human Services, the Department of Veterans Affairs, and educational, professional, and interdisciplinary associations and organizations involved in the health care of older adults (including, but not limited to, the Association of American Medical Colleges, the American Association of Colleges of Nursing, the National Association of Social Workers, the American Psychological Association, and the American Public Health Association) should develop and disseminate core competencies, curricula, and continuing education opportunities, including for primary care providers, that focus on cognitive aging as distinct from clinical cognitive syndromes and diseases, such as dementia.

Recommendation 7: ***Promote Cognitive Health in Wellness and Medical Visits***

Public health agencies (including the Centers for Disease Control and Prevention and state health departments), health care systems (including the Veterans Health Administration), the Centers for Medicare & Medicaid Services (CMS), health insurance companies, health care professional schools and organizations, health care professionals, and individuals and their families should promote cognitive health in regular medical and wellness visits among people of all ages. Attention should also be given to cognitive outcomes during hospital stays and post-surgery.

Specifically, health care professionals should use patient visits to:

- identify risk factors for cognitive decline and recommend measures to minimize risk; and review patient medications, paying attention to medications known to have an impact on cognition;
- provide patients and families with information on cognitive aging (as distinct from dementia) and actions that they can take to maintain cognitive health and prevent cognitive decline; and
- encourage individuals and family members to discuss their concerns and questions regarding cognitive health.

In addition, other components of the health care system have a cognitive health promotion role:

- CMS should develop and implement demonstration projects to identify best practices for clinicians in assessing cognitive change and functional impairment and in providing appropriate counseling and prevention messages during, for example, the Medicare Annual Wellness Visit or other health care visits.
- Health care systems and private and public health insurance companies should develop evidence-based programs and materials on cognitive health across the life span.
- During and after hospital stays and post-surgery, health care providers, patients, and families should be alert to potential cognitive changes and delirium.

Recommendation 8: ***Develop Consumer Product Evaluation Criteria and an Independent Information Gateway***

The Centers for Disease Control and Prevention, National Institutes of Health, and the Administration for Community Living, in conjunction with other health and consumer protection agencies, nonprofit organizations, and professional associations, should develop, test, and implement cognitive aging information resources and tools that can help individuals and families make more informed decisions regarding cognitive health.

Specifically,

- A central, user-friendly, easily navigated website should be available to provide independent, evidence-based information and links relevant to cognitive aging, including information on the promotion of protective behaviors and links to effective programs and services. The information should be presented in a way that takes health literacy into account.
- Consumer-relevant criteria should be developed and widely disseminated to provide individuals and families with guidance on evaluating cognition-related products (e.g., cognitive training products, nutriceuticals, and medications).

Recommendation 9: ***Expand Services to Better Meet the Needs of Older Adults and Their Families with Respect to Cognitive Health*** **Relevant federal and state agencies (including the Administration for Community Living [ACL], the Centers for Disease Control and Prevention [CDC], the National Highway Traffic Safety Administration [NHTSA], and the Consumer Financial Protection Bureau), nonprofit organizations (such as the Financial Industry Regulatory Authority), professional associations, and relevant private-sector companies and consumer organizations should develop, expand, implement, and evaluate programs and services used by older adults relevant to cognitive aging with the goal of helping older adults avoid exploitation, optimize their independence, improve their function in daily life, and aid their decision making.**

Specifically,

- Financial decision making:
    - The banking and financial services industries and state and federal banking and financial regulators should develop and disseminate banking and financial policies, services, and information materials that assist older adults and their families in making decisions that meet their financial means and objectives, that reduce the opportunities for unsuitable decisions, and that mitigate the harms of such decisions.
    - Surrogacy mechanisms, such as powers of attorney or multiparty accounts, should have appropriate safeguards to protect the interests of the older adult.
    - The financial services industries and relevant state and federal agencies should develop, strengthen, and implement systems approaches, best practices, training, and laws and regulations to help verify that financial transactions are not fraudulent or the result of diminished capacity or undue influence.
    - Systems should be strengthened for reporting or taking other protective actions against potential financial fraud, exploitation, or abuse to relevant enforcement and investigative officials. Laws and regulations should be revised to mitigate civil liability and professional harms resulting from such protective actions.
- Driving and transportation:
    - NHTSA, states' departments of motor vehicles, and relevant professional and consumer organizations such as the American Automobile Association should expand, validate, and disseminate tools and informational materials to assist older adults in maintaining and assessing their driving skills and to assist older adults and their families in making decisions about safe driving.
    - The automobile industry should expand and evaluate technologies that enhance decision making and safety for older drivers.
    - State and local transportation authorities, local planning commissions, private developers, and community groups should expand efforts to develop and implement alternative transportation options to accommodate changes that occur with cognitive aging, including efforts to ensure safe and walkable communities.
- Technology:
    - Technology industries should develop and adapt hardware, software, and emerging technologies to accommodate the needs of older adults that are related to cognitive aging.
    - The CDC, ACL, and other relevant agencies, organizations, and private-sector companies should support evidence-based programs that educate older adults in the use of emerging technologies.
- Health information:
    - Health information providers, including private-sector companies and government agencies, should ensure that their websites (including patient health portals), packaging (including medication packaging), and other consumer health information relevant to cognitive aging meet health literacy standards.

Recommendation 10: ***Expand Public Communication Efforts and Promote Key Messages and Actions***

The Centers for Disease Control and Prevention, the Administration for Community Living, the National Institutes of Health, other relevant federal agencies, state and local government agencies, relevant nonprofit and advocacy organizations and foundations, professional societies, and private-sector companies should develop, evaluate, and communicate key evidence-based messages about cognitive aging through social marketing and media campaigns; work to ensure accurate news and

storylines about cognitive aging through media relations; and promote effective services related to cognitive health in order to increase public understanding about cognitive aging and support actions that people can do to maintain their cognitive health.

Public communications efforts should:

- Reach the diverse U.S. population with campaigns and programs targeted to all relevant groups;
- Be sensitive to existing differences in knowledge, literacy, health literacy, perceived risk, cognitive aging–related behavior, communication practices, cultures and beliefs, speech and hearing declines, and skills and self-efficacy among target groups;
- Include evaluation components to assess outreach efficacy in the short and long term, and research the optimal communication strategies for the key messages among the target groups;
- Be updated as new evidence is gained on cognitive aging;
- Emphasize a lifelong approach to cognitive health;
- Promote succinct and actionable key messages that are understandable, memorable, and relevant to the target groups;
- Focus on sustaining changes in behaviors that promote cognitive health; and
- Promote effective evidence-based tools for maintenance of cognitive health and cognitive change assessment, as well as the information gateway on cognitive aging (see Recommendation 8).

McKnight Brain Research Foundation
Abbreviated History
July 2023

1. Established by Evelyn F. McKnight through a Trust Agreement dated May 26, 1999. Henry H. Raattama, Jr., Esquire, represented Mrs. McKnight.

2. Purpose: ***"…to provide support for medical research of the brain to accomplish alleviation of memory loss of the aging, including making grants to charitable organizations involved in such research."***

3. The trustee agreement specified three named "founding" trustees and one corporate trustee.
   Founding Trustees:
   A. J. Lee Dockery, M.D., retired obstetrician and gynecologist, medical administrator and educator.
   B. Nina Ellenbogen Raim, M.D., J.D., retired pediatrician, and attorney.
   C. Michael L. Dockery, M.D., practicing orthopedic surgeon.
   D. SunTrust Bank, Corporate Trustee.

4. June 25, 1999 -- Trust Document amended to specify a minimum of three trustees and a maximum of five trustees plus one corporate trustee.

5. April 28, 2000 -- First Gift Agreement for the MBRF with the University of Florida included a match by the State of Florida creating an endowment.

6. May 1, 2004 -- Second Gift Agreement for the MBRF with the University Alabama at Birmingham.

7. April 2005 -- "Qualifications for New Trustee" were adopted unanimously by the trustees. (The most current version of this document is included in the orientation packet.)

8. May 6, 2006—Approved a Research Partnership in Cognitive Aging between the McKnight Brain Research Foundation and the National Institute on Aging (NIA) through the Foundation for the National Institutes of Health (FNIH) to support a grant making program supporting research in age-related cognitive decline and memory loss. The Research Partnership in Cognitive Aging was approved for five years with a commitment of funding by the MBRF of $5 million payable $1 million annually and a minimum of $5 million from NIA, payable $1 million annually.

9. October 17, 2006 -- Third Gift Agreement for the MBRF with the University of Arizona.

10. December 24, 2006 – Fourth Gift Agreement for the MBRF with the University of Miami.

11. January 1, 2006 -- John G. Clarkson, M.D., was appointed as the fourth trustee. Dr. Clarkson was previously senior vice president for medical affairs and dean of the University of Miami Leonard M. Miller School of Medicine, and former director of UM's the Bascom Palmer Eye Institute and chairman of the Department of Ophthalmology. (Mr. and Mrs. McKnight had made a large gift to the Bascom Palmer Eye Institute to establish the William L McKnight Vision Research Center.)

12. April 1, 2009 -- Judith A. Salerno, M.D., M.S., was appointed as the fifth trustee. (Dr. Salerno was the former director of the National Institute on Aging and, in 2009, was the current Leonard D. Schaeffer Executive Officer of the Institute of Medicine of the National Academies.)

13. July 20, 2011 -- Dr. Clarkson's resignation was accepted by the trustees.

14. April 1, 2012 -- Dr. Salerno's second term was not renewed by the trustees.

15. April 11, 2012 -- Gene Ryerson, M.D., was appointed trustee replacing Dr. Clarkson. (Dr. Ryerson is a retired professor in pulmonary medicine from the University of Florida and the recipient of many outstanding teaching awards by the medical students.)

16. August 8, 2012 -- Robert M. Wah, M.D., was elected to replace Dr. Salerno as fifth trustee. Dr. Wah is a reproductive endocrinologist and obstetrician and gynecologist and, in 2012, was the Chief Medical Officer of North American Public Sector and Vice President of North American Public Sector at DXC Technology Company. Robert was President of the American Medical Association from June 2014-June 2015.

!7. October 31, 2012—Approved the extension of the contract for the Research partnership in Cognitive aging for another five years under the same financial commitments of $5 million by the MBRF payable at $1million annually and a minimum of $5 million from the NIA also payable $1 million annually.

18. October 14, 2014 -- The trustees voted to abolish the consensus form of board governance and to establish a Board Chair, Vice Chair and Secretary position.

A. Dr. Lee Dockery was elected Board Chair.
B. Dr. Michael Dockery was elected Vice Chair.
C. Ms. Cianciotto, Corporate Trustee, to serve as the Secretary.

Terms of Office:

1. Two years of active service as a trustee member are required before becoming an officer.
2. An individual eligible to serve as an officer may be nominated by another trustee or self-nominate.
3. The term of office coincides with the fiscal year.
4. The term of the office of the chair is two years, but the number of terms not limited.

19. February 15, 2015--Trust Document amended to specify a minimum of three trustees and a maximum of seven trustees plus one corporate trustee.

20. April 29, 2015 -- Dr. Gene Ryerson was unanimously re-elected MBRF Trustee for a second three-year term.

21. August 12, 2015 -- Madhav Thambisetty, M.D., Ph.D., a neurologist and clinical pharmacologist was elected sixth trustee. Dr. Thambisetty is also director of Clinical and Translational Neuroscience within the Laboratory of Behavioral Neuroscience at the NIA and is an adjunct associate professor of neurology at the John's Hopkins University School of Medicine in Baltimore, Maryland.

22. August 12, 2015 -- Robert M. Wah, M.D., was unanimously re-elected MBRF Trustee for a second three-year term

23. April 27, 2016 -- Richard S. Isaacson, MD, a clinical neurologist and distinguished medical educator was elected seventh trustee. Dr. Isaacson currently serves as Director of the Neurology Residency Training Program and Director of the Alzheimer's Prevention Clinic, Weill Cornell Memory Disorders Program and Associate Professor of Neurology at Weill Cornell Medicine and New York-Presbyterian. Prior to his move to Cornell, Dr. Isaacson was Associate Professor of Clinical Neurology, Vice Chair of Education, and Education Director of the McKnight Brain Institute in the Department of Neurology at the University of Miami (UM) Leonard M. Miller School of Medicine.

24. April 5, 2017 -- The Trustees approved the funding of two Clinical Translational Scholars per year with the American Academy of Neurology (AAN) through the American Brain Research Foundation. Each scholarship is for a period of two years for a total of $150,000 with an additional $30,000 administrative cost payable to the American Brain Foundation. The name of the scholarship is the McKnight Clinical Translations Research Scholarship in Cognitive Aging and Age-related Memory Loss.

25. June 1, 2017 -- The contract was signed between the American Brain Foundation and the MBRF for the recruitment and management of the McKnight Clinical Translation Research Scholarship program.

26. February 21, 2018 -- Susan L. Pekarske, M.D., a clinical pathologist with a specialty in hematology was elected as trustee. The effective date of Dr. Pekarske's appointment was undetermined at the time subject to her personal commitments and the terms of service of the existing trustees within the MBRF.

27. April 1, 2018 -- Amy Porter was appointed executive director of the MBRF. Amy has served as a non-profit professional for over 30 years with 16 years' experience serving as executive director and CEO of two national, health-related organizations – the Foundation for the National Institutes of Health (FNIH) from 2001-2010 and the National Osteoporosis Foundation (NOF) from 2010 through 2017.

28. April 4, 2018 -- Dr. Gene Ryerson was unanimously re-elected MBRF Trustee for a third and final three-year term.

29. May 8, 2018 -- The Trust Document was amended to specify a minimum of seven trustees and a maximum of eleven trustees plus one corporate trustee.

30. July 1, 2018 -- Dr. Pekarske began her first three-year term of service as trustee of the MBRF.

31. July 16, 2018 -- Dr. Robert Wah was unanimously re-elected MBRF Trustee for a third and final three-year term.

32. July 16, 2018 -- Dr. Madhav Thambisetty was unanimously re-elected MBRF Trustee for a second three-year term.

33. October 23, 2018 -- Research Partnership in Cognitive Aging III contract was renewed with the National Institute on aging through the Foundation or the National Institutes of Health. The third research partnership project will jointly fund research to "Establish a Network for Identification, Evaluation and Tracking of Older Persons with Superior Competent Performance for their Chronological Age.

34. October 30, 2018 -- The Board of Trustees approved a reorganization plan to establish five standing committees of the Board to operationalize the activities and responsibilities of the Board. The following committees were established with each to be chaired by a trustee appointed by the Chair of the Board.

Chair of the Board. Each trustee is expected to serve on at least one standing committee. (This was changed to "expected to serve on at least two committees" on July 22, 2020.)

1. Membership and Governance
2. Finance
3. Education
4. Research
5. Communications

35. July 25, 2018 -- Dr. Lee Dockery was unanimously re-elected to a two-year term as Chair. Dr. Michael Dockery is unanimously re-elected to a two-year term as Vice Chair.

36. October 30, 2018 -- The Trustees approved a two-year communications plan with a budget not to exceed $300,000 which included the services of Valerie Patmintra, senior communication advisor.

37. April 10, 2019 -- Dr. Lee Dockery, founding trustee and Chair of the Board of Trustees of the MBRF, retired and was elected Chair Emeritus.

38. April 10, 2019 -- Dr. Michael L. Dockery, founding trustee and formerly Vice Chair of the MBRF was elected as the new Chair. Election to fill the vacant Vice Chair position was delayed until the July 2019 meeting of the trustees.

39. April 10, 2019 -- Nina Ellenbogen Raim, M.D., J.D., founding trustee of the MBRF resigned as trustee and was elected Trustee Emerita as an honorary status without specific duties and without compensation.

40. April 10, 2019 -- Dr. Richard Isaacson was unanimously re-elected MBRF Trustee for a second three-year term.

41. July 31, 2019 -- Dr. Madhav Thambisetty was unanimously elected as Vice Chair for a two-year term.

42. October 23, 2019 -- Funding was approved for the Evelyn F. McKnight Neurocognitive Post-Doctoral Fellowship at the University of Miami at $100,000 per year for a total of two years.

43. February 5, 2020 -- The trustees approved up to two mid-career research investigator awards. The *McKnight Brain Research Foundation Mid-Career Research Award in Cognitive Aging and Memory Loss will* focus on the "mature end of the spectrum" of clinical research and human studies. Funding will be available to researchers outside the MBIs as well as to those within the MBIs. Each year, one award will be made to support studies focusing on clinical translational research and another towards understanding basic biological mechanisms underlying cognitive aging and age-related memory loss. The awards will be up to $250,000 per year, per investigator, for three years from the MBRF to be matched by the host institution in equal amounts.

44. February 5, 2020 -- The trustees approved the recommendation for the education committee to be responsible for identifying and developing informational resources to be made available to primary care providers and the public.

45. February 5, 2020 -- The trustees approved the additional budget request from the University of Arizona to support additional requirements for resubmission of the Precision Aging Network Pilot Proposal not to exceed $250,000.

46. October 1, 2020 – Dr. Patricia Boyle was unanimously elected to her first term as Trustee.

47. October 14, 2020 -- The trustees approved renewal of the partnership with the American Brain Foundation for 5-years with a $1,650,000 grant to support 10 additional McKnight Clinical Translational Research Scholarships from 2023 – 2028.

48. November 1, 2020 – Dr. Allison Brashear was unanimously elected to her first term as Trustee.

49. February 26, 2021 -- The trustees approved the renewal contract with the American Brain Foundation for the administration and management of the of McKnight Cognitive Aging and Memory Clinical Translation Research Scholarship in Cognitive Aging and Age-Related memory Loss through the American Academy of Neurology.

50. February 26, 2021 -- The trustees approved the American Federation for Aging Research (AFAR) for the management and administration for the Mid-Career Investigator Awards.

51. April 9, 2021 -- The contract was signed with American Federation for Aging Research

52. April 30, 2021 -- Added the word "Innovator" to the Mid-Career Awards – the name is the ***McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss.***

53. April 30, 2021 -- Gene Ryerson, MD, completed his third and final term as trustee of the MBRF. Dr. Ryerson received a proclamation and an inscribed Tiffany Crystal Bowl in recognition of nine years of dedicated service to the MBRF.

54. July 28, 2021 -- Robert M. Wah, MD, completed his third and final term as trustee of the MBRF. Dr. Wah received a Proclamation and an inscribed display cabinet for medals in recognition of nine years of dedicated service to the MBRF.

55. October 23, 2019 -- The trustees approved a proposal for a one-time funding in the amount of $200,000 to launch the *Evelyn F. McKnight Neurocognitive Post-Doctoral Fellowship*. The grant is for $100,000 annually for a period of two years for a total not to exceed $200,000.

56. October 28, 2021 -- The trustees approved a one-time funding to establish the *Evelyn F. McKnight Neurocognitive Clinical Scholar in Brain Health and Aging* postdoctoral training program in the amount of $250,000 to be matched by the University of Miami. The grant is for $50,000 annually for a period of five years for a total not to exceed $250,000 with the understanding recruitment for the scholars will be from a national qualified applicant pool and efforts would be made to retain the successful scholars as clinical science faculty.

57. December 7, 2021 –John E. Brady, MD, was unanimously elected to the Board of Trustees for a three-year appointment to begin January 1, 2022.

58. February 1, 2022--Amy Porter, executive director of the MBRF, since April 1, 2018, announced her intended retirement by December 31, 2022, but not later than the end of her contract year, April 1, 2023.

59. March 23, 2022—The Membership and Governance Committee requested approval by the Trustees of the concept of hiring an Educational Advisor to advance the educational outreach initiative to Primary Care Provider (PCP) similar to the function of the MBRF Senior Communications Advisor. After discussion, the Trustees approved the development of and RFA for an education advisor consultant to assist the MBRF in understanding the educational environment in defining the scope of what the MBRF can or hope to accomplish with an Education Initiative and the required credentials for an Education Advisor.

60. August 15, 2022 -- Angelika Schlanger, PhD, was appointed as executive director of the MBRF. Dr. Schlanger served with distinction as the inaugural director of the Frederick A. DeLuca Foundation for four years prior to joining the MBRF.

61. October 1, 2022 -- Amy Porter officially retired from her position as the first executive director of the MBRF.

62. September 20, 2022—After review of several requested proposal from different organizations, the Trustees approved the engagement of the Strategic Communications and Planning, Inc. (SCP) agency to expand the educational outreach on age related cognitive decline and memory loss to Primary Care Providers and the consumer with a budget not to exceed $40,000.

Specifically, the SCP proposal was designed to**:**

- Conduct a landscape analysis of the educational resources and assessment tools available to primary care providers (PCPs) related to cognitive aging and brain health; and
- Make a series of specific, short-, mid- and long-term recommendations that MBRF can pursue to encourage PCPs to make brain health assessments and education a more regular part of their practices and educate the consumer about the importance of brain health integrated within personal health maintenance behavior.

63. February 16, 2023-- Strategic Communications and Planning, Inc (SCP) presented report to Board of Trustees.62. February 16, 2023--The Trustees authorized the Executive Director to proceed with outreach to organizations aligned with existing education efforts directed to consumers/patients, and those directed to Primary Care Provides (PCPs).

64. February 16, 2023--The trustees authorized the Executive Director to pursue the recommended strategies #1 (Consumer Health/Consumer Education Initiative) and #2 (Primary Care Education and Practice Models/Approaches) from the SCP Scoping Document and to incorporate strategy #3 (PCP Public Information Campaign) within a three-year communications plan.

65. March 31, 2023 -- Richard S. Isaacson, MD, after seven years of dedicated service resigned his position as trustee of the MBRF.

66. April 17, 2023—Sharon Brangman, MD and Roy H. Hamilton, MD, MS are unanimously elected to the Board of Trustees for three-year appointment to begin July 1, 2023

67. May 3, 2023—After intensive review of five proposals for a Public Information Campaign for Primary Care Providers, the BRG Communications Agency was selected to manage the project to enhance and expand a three-year communications plan at a budget level of $1.75 million over the three years, including consulting fees.

69. May 3, 2023--The Trustees reviewed proposals from aligned organizations with existing educational programs and curricula interested in partnering with the MBRF by using the MBRF Key Messages in developing a stand-along brain health module or incorporate the module into existing curricula designed for consumers and patients.

70. May 3, 2023—After discussion, the Trustees recommended the Self-Management Resource Center (SMRC) be invited to submit a concept paper or proposal and budget for the partnering with the MBRF in the development of educational materials in brain health directed toward patients and consumers.

The Self-Management Resource Center is the culmination of 40 years of research and program development, all focused on the goal of helping people better manage their chronic health conditions.

71. A Proclamation to Richard S. Isaacson, MD recognizing his seven years of service to the MBRF was presented and read into the minutes of May 3, 2023 Trustees' meeting.

Duties and Responsibilities
of
Individual Trustees

McKnight Brain Research Foundation (MBRF)
Board of Trustees
Individual Trustee Duties and Responsibilities

Duties: To advise, govern, oversee policy and direction, and assist with the leadership and promotion of the McKnight Brain Research Foundation (MBRF) in support of the organization's vision, mission and goals. As a board member, passion, participation and commitment are vital to the success of the Foundation. A board member's effectiveness will be enhanced by striving to be knowledgeable about the trends and research initiatives in cognitive aging and associated memory loss in the aging.

Responsibilities: Leadership, Governance and Oversight:

1. Understand and support the Vision, Values, and Mission of the MBRF.
2. Adhere to the Code of Ethics, avoid or report Conflicts of Interest.
3. Understand and review periodically the Policies and Procedures of the MBRF.
4. Review agenda, financial information, and supporting material in advance of the trustee meetings or committee meetings.
5. Ensure fiscal oversight and integrity with review and approval of the MBRF annual operating budget, major expenditures, investment of funds, and any related financial responsibilities.
6. Provide oversight of the MBRF; monitor and evaluate the effectiveness of funded institutes and programs through a regular review, completed at least on a yearly basis.
7. Serve as an advocate for the MBRF and foster collegial relationships with its institutes and partners, the scientific community, and state and federal officials.
8. Attend and participate in all MBRF trustee meetings – usually four a year – focusing attention on the discussion and matters at hand.
9. Attend and participate as a member of at least two committees of the Board of Trustees.
10. Ensure that each topic on the meeting agenda receives sufficient attention and that communication is collegial and contributes to the effectiveness and cohesiveness of the group.
11. Respond in a timely manner (within 2 business days) to emails from other Trustees or staff regarding ongoing assignments, work of the committees, reviews, reports or voting by email.
12. Identify and share names of individuals with relevant skills and experience to be considered as potential nominees for Trustee positions; and share names of organizations and foundations which may be potential program or funding partners with the MBRF.
13. At the direction of the MBRF Chair, act as representative or spokesperson for the MBRF to partners or other constituencies; take advantage of opportunities to enhance the organization's public image through interviews, content for the MBRF website, presentations, and highlighting your role as a Trustee.
14. Monitor and provide feedback, insights, or direction as requested or needed. Maintain a good working relationship with other Trustees, the Corporate Trustee, the Executive Director and staff and advisors.
15. Participate in setting annual goals for the MBRF, in strategic planning, vision setting, and evaluation efforts.

Length of Term: Three (3) years, which may be renewed for additional terms, pending approval of the Board of Trustees, for a maximum of nine (9) years.

Approved April 6, 2015
Length of Term Approved July 31, 2019, Trustees Meeting
Responsibilities Amended and Approved July 22, 2020, Trustees Meeting

McKnight Brain Research Foundation (MBRF)
Code of Ethics

The McKnight Brain Research Foundation is committed to:

- Act honestly, truthfully and with integrity in all transactions and dealings.
- Promote the avoidance of conflicts of interest and commit to the appropriate handling of actual or apparent conflicts of interest in all relationships.
- Treat all grantees fairly and treat every individual with dignity and respect.
- Be a good corporate citizen and to comply with both the spirit and the letter of the law.
- Act responsibly toward the professional communities in which we work and for the benefit of the professional communities we serve.
- Be responsible, transparent, and accountable for all of our actions.
- Attend all regularly scheduled board meetings insofar as possible, and become informed concerning the issues to be considered at those meetings.
- Endeavor to make policy decisions only after full discussion.
- Render all decisions based on the available facts and independent judgment, and refuse to surrender that judgment.
- Encourage the free expression of opinion by all board members, and seek systematic communications among the board members.
- Work with other board members to establish effective board policies and to delegate authority as appropriate.
- Stay informed about pertinent issues by individual study and through participation in programs providing needed information relevant to the MBRF.
- Take no private action that will compromise the Foundation, and respect the confidentiality of information that is privileged under applicable law.
- Monitor and evaluate on a regular basis the MBRF actions and activities.
- Ensure that the resources of the Foundation are responsibly and prudently managed.
- Adopt and monitor spending practices and investment policies which are fair, reasonable and appropriate to fulfill the mission of the Foundation.

Adopted May 18, 2005
Reaffirmed July 22, 2020

McKnight Brain Research Foundation
Conflict of Interest Policy

ARTICLE I
Purpose

The purpose of this Conflict of Interest Policy is to protect the interest of the McKnight Brain Research Foundation ("MBRF") when it is contemplating entering into a transaction that may benefit the private interest of a MBRF Trustee. This Conflict of Interest Policy is intended to supplement, but not replace, any applicable state and federal laws governing conflicts of interest applicable to MBRF including, specifically, Section 617.0832, Fla. Stat. and Section 4941 of the Internal Revenue Code of 1986, as amended.

ARTICLE II
Conflict of Interest

A Trustee has a conflict of interest with respect to a proposed transaction if completion of the transaction would directly or indirectly benefit the Trustee or an affiliate of the Trustee. Benefit for this purpose means a financial benefit. Affiliate for this purpose means all members of the Trustee's immediate family or a business entity 35% or more of which is owned by the Trustee.

ARTICLE III
Disclosure

If a Trustee has an interest in a possible transaction, such interest shall be disclosed to all Trustees ("Disclosing Trustee"). The Trustees, other than the Disclosing Trustee, shall decide whether the transaction giving rise to the potential conflict is, on balance, in the best interest of MBRF. The Trustees shall be free to consult with the Disclosing Trustee to fully understand the proposed transaction and the circumstances giving rise to the conflict.

After full disclosure and appropriate due diligence, the Trustees, other than the Disclosing Trustee, shall vote on the transaction using the same criteria for approval or disapproval as is used for any transaction. If the Trustees believe the transaction to be in the best interest of MBRF, the Trustees shall be free to approve the proposed transaction notwithstanding the conflict.

ARTICLE IV
Customary Business Practices

In no event shall receipt of a benefit that is a customary business practice be considered a conflict. A customary business practice means a business related gift, such as a meal, of a type customarily provided in the context within which the business related gift is provided.

ARTICLE V
Compensation

It is recognized the setting of Trustee compensation by Trustees is an inherent conflict. Because of the MBRF organizational structure, it is not possible to cause compensation to be decided by independent trustees. In recognition of this inherent conflict, the Trustees shall annually review Trustee compensation and the basis used to establish Trustee compensation. The Trustees will research available comparables, if any, and such other third party information as is reasonably available. The Trustees shall record the basis for compensation and the amount of compensation.

ARTICLE VI
Annual Filing

Each member of the Board of Trustees shall file a statement annually setting forth any conflict of interest which might occur during the ensuing year. The statement shall disclose as fully as possible the nature of the potential conflict and the nature of the Trustees' interest in the possible transaction. The statements shall be circulated to all Trustees.

McKNIGHT BRAIN RESEARCH FOUNDATION
TRUSTEES' CONFLICT OF INTEREST STATEMENT

I have read the McKnight Brain Research Foundation Conflict of Interest Policy adopted by the Board of Trustees on the eighteenth of May, 2005. I agree to answer any questions the Board of Trustees may have with respect to any actual or potential conflict of interest and to otherwise abide by the Conflict of Interest Policy.

Check one of the following:

____ To the best of my knowledge, there exists no circumstances involving me or an affiliate that may be considered an interest in a transaction or possible transaction to be entered into by the McKnight Brain Research Foundation.

or

____ There does exist the following conflict of interest in a possible transaction:

_____

_____
Signature

_____
Date

McKnight Brain Research Foundation (MBRF)

Annual Trustee Responsibilities and Commitment Form

Trustee Name_____Year_____

Vision:

To: "Improve the quality of life through the understanding and alleviation of age-related memory loss."

Value Statement:

- ***Commitment***

The MBRF is committed to its vision to understand and alleviate age-related memory loss, and expects the same of its grant recipients and research partners.

- ***Discovery***

The MBRF values scientific curiosity and discovery leading to clinical intervention in age-related memory loss.

- ***Honesty/Integrity***

The MBRF conducts its affairs with the highest degree of honesty, integrity, and accountability and expects the same of others.

Mission:

Lead in generating interest and support of scientific research to understand and alleviate age-related memory loss.
Inspire commitment and shared vision in the understanding and alleviation of age-related memory loss.
Nurture scientists dedicated to the exploration of innovative research initiatives intended for clinical application in age-related memory loss.
Promote collaboration and communication among research scientists, institutions, and organizations engaged in research in age-related memory loss.
Partner with research scientists, institutions, and organizations to promote research to understand and alleviate age-related memory loss.
Recognize and Reward significant achievement in discoveries leading to clinical intervention to understand and alleviate age-related memory loss.

Code of Ethics

The McKnight Brain Research Foundation is committed to:

- Act honestly, truthfully and with integrity in all transactions and dealings.
- Promote the avoidance of conflicts of interest and commit to the appropriate handling of actual or apparent conflicts of interest in all relationships.
- Treat all grantees fairly and treat every individual with dignity and respect.
- Be a good corporate citizen and to comply with both the spirit and the letter of the law.
- Act responsibly toward the professional communities in which we work and for the benefit of the professional communities we serve.
- Be responsible, transparent, and accountable for all of our actions.
- Attend all regularly scheduled board meetings insofar as possible, and become informed concerning the issues to be considered at those meetings.
- Endeavor to make policy decisions only after full discussion.
- Render all decisions based on the available facts and independent judgment, and refuse to surrender that judgment.
- Encourage the free expression of opinion by all board members, and seek systematic communications among the board members.
- Work with other board members to establish effective board policies and to delegate authority as appropriate.
- Stay informed about pertinent issues by individual study and through participation in programs providing needed information relevant to the MBRF.

Code of Ethics, Continued

- Take no private action that will compromise the Foundation, and respect the confidentiality of information that is privileged under applicable law.
- Monitor and evaluate on a regular basis the MBRF actions and activities.
- Ensure that the resources of the Foundation are responsibly and prudently managed.
- Adopt and monitor spending practices and investment policies which are fair, reasonable and appropriate to fulfill the mission of the Foundation.

I understand my duties and responsibilities as a Trustee are to:

1. Understand and support the Vision, Values, and Mission of the MBRF.
2. Adhere to the Code of Ethics, avoid or report Conflicts of Interest.
3. Understand and review periodically the Policies and Procedures of the MBRF.
4. Review agenda, financial information, and supporting material in advance of the trustee meetings or committee meetings.
5. Ensure fiscal oversight and integrity with review and approval of the MBRF annual operating budget, major expenditures, investment of funds, and any related financial responsibilities.
6. Provide oversight of the MBRF; monitor and evaluate the effectiveness of funded institutes and programs through a regular review, completed at least on a yearly basis.
7. Serve as an advocate for the MBRF and foster collegial relationships with its institutes and partners, the scientific community, and state and federal officials.
8. Attend and participate in all MBRF trustee meetings – usually four a year -- focusing attention on the discussion and the matters at hand.
9. Attend and participate as a member of at least two committees of the Board of Trustees.
10. Ensure that each topic on the meeting agenda receives sufficient attention and that communication is collegial and contributes to the effectiveness and cohesiveness of the group.
11. Respond in a timely manner (within 2 business days) to emails from other Trustees or staff regarding ongoing assignments, work of the committees, reviews, reports or voting by email.
12. Identify and share names of individuals with relevant skills and experience to be considered as potential nominees for Trustee positions; and share names of organizations and foundations which may be potential program or funding partners with the MBRF.
13. At the direction of the MBRF Chair, act as representative or spokesperson for the MBRF to partners or other constituencies; take advantage of opportunities to enhance the organization's public image through interviews, content for the MBRF website, presentations, and highlighting your role as a Trustee.
14. Monitor and provide feedback, insights, or direction as requested or needed. Maintain a good working relationship with other Trustees, the Corporate Trustee, the Executive Director and all other staff and advisors.
15. Participate in setting annual goals for the MBRF, in strategic planning, vision setting and evaluation efforts.

I accept the above commitment as an understanding of my role and responsibilities as a member of the Board of Trustees.

Signature_____ Date_____

McKnight Brain Research Foundation (MBRF)

Annual Trustee Self-Assessment

Vision:

To: "Improve the quality of life through the understanding and alleviation of age-related memory loss."

Trustee Name_____Year_____

Previously, I committed to executing my responsibilities as a Trustee of the MBRF to the following areas. Now, I'm using a scale of 1 to 3 with 3 representing excellence and leadership; 2 as needing more of my attention and/or greater involvement; and 1 as having not met the responsibilities and requirements of the role of Trustee.

I understand that my evaluation will be shared with the MBRF Chair and the Chair of the Membership and Governance Committee. I welcome their suggestions for how best to expand my understanding of and participation in the work of the MBRF and to uphold its Vision, Values, Mission and Code of Ethics.

As a Trustee, I:	Score 1 – 3
1. Understand and support the Vision, Values, and Mission of the MBRF.	
2. Adhere to the Code of Ethics, avoid or report Conflicts of Interest.	
3. Understand and review periodically the Policies and Procedures of the MBRF.	
4. Review agenda, financial information, and supporting material in advance of the trustee meetings or committee meetings.	
5. Ensure fiscal oversight and integrity with review and approval of the MBRF annual operating budget, major expenditures, investment of funds, and any related financial responsibilities.	
6. Provide oversight of the MBRF; monitor and evaluate the effectiveness of funded institutes and programs through a regular review, completed at least on a yearly basis.	
7. Serve as an advocate for the MBRF and foster collegial relationships with its institutes and partners, the scientific community, and state and federal officials.	
8. Attend and participate in all MBRF trustee meetings – usually four a year -- focusing attention on the discussion and the matters at hand.	
9. Attend and participate as a member of at least two committees of the Board of Trustees.	
10. Ensure that each topic on the meeting agenda receives sufficient attention and that communication is collegial and contributes to the effectiveness and cohesiveness of the group.	

11. Respond in a timely manner (within 2 business days) to emails from other Trustees or staff regarding ongoing assignments, work of the committees, reviews, reports or voting by email.	
12. Identify and share names of individuals with relevant skills and experience to be considered as potential nominees for Trustee positions; and share names of organizations and foundations which may be potential program or funding partners with the MBRF.	
13. At the direction of the MBRF Chair, act as representative or spokesperson for the MBRF to partners or other constituencies; take advantage of opportunities to enhance the organization's public image through interviews, content for the MBRF website, presentations, and highlighting your role as a Trustee.	
14. Monitor and provide feedback, insights, or direction as requested or needed. Maintain a good working relationship with other Trustees, the Corporate Trustee, the Executive Director and all other staff and advisors.	
15. Participate in setting annual goals for the MBRF, in strategic planning, vision setting and evaluation efforts.	

I acknowledge that in the areas in which I ranked less than a 3, it will be desirable for me to improve my performance through greater attention, involvement, and understanding. I commit to taking the following steps to improve in these areas. As needed, I will identify the areas in which I would benefit from additional information or mentoring to improve my performance. I look forward to a review of my participation and performance with the MBRF Chair.

_____

_____

_____

_____

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_____

I have the following suggestions for how the Board of Trustees might improve:

_____

_____

_____

_____

_____

_____ _____

Signature Date

McKnight Brain Research Foundation
Expense Reimbursement Policy

Trustee Reimbursement

The Trustees of the McKnight Brain Research Foundation (MBRF) will be reimbursed for any out of pocket expenses and travel costs associated with MBRF business.

1. Trustees will submit a MBRF Expense Report form when requesting reimbursement.
2. Trustees are responsible for providing receipts when requesting reimbursement for out of pocket documented expenses and travel costs associated with MBRF business.
3. Reimbursement should be requested within 60 days of the expense occurrence.
4. The MBRF Expense Report form and receipts should be sent to the Corporate Trustee for processing.

Executive Director Reimbursement

The Executive Director of the McKnight Brain Research Foundation (MBRF) will be reimbursed for any out of pocket expenses and travel costs associated with MBRF business.

1. The Executive Director will submit a MBRF Expense Report form when requesting reimbursement.
2. The Executive Director is responsible for providing receipts when requesting reimbursement for out of pocket documented expense and travel costs associated with MBRF business.
3. Reimbursement should be requested within 60 days of the expense occurrence.
4. The MBRF Expense Report form and receipts should be sent to the Corporate Trustee for processing.

Inter-Institutional Meeting Attendee Reimbursement

Attendees and invited guests will be reimbursed for any out of pocket documented expenses and travel costs associated with attending the Inter-Institutional Meeting. Reimbursement will not be provided for the following:

Rental Cars
Meals when a meal was provided as part of the meeting

1. Attendees will submit a Travel Expense Reimbursement form when requesting reimbursement.
2. Attendees are responsible for providing receipts when requesting reimbursement for out of pocket documented expenses and travel costs associated with attending the Inter-Institutional Meeting.
3. Reimbursement should be requested within 14 days following the conclusion of the Inter-Institutional Meeting.
4. The Travel Expense Reimbursement form and receipts should be sent to the Corporate Trustee for processing.

Failure to comply with this policy will result in no reimbursement of expenses.

Policy adopted July 31, 2019

Duties and Responsibilities of Officers and Executive Director

Chair of the Board of Trustees

McKnight Brain Research Foundation

The role of the Chair of the Board of Trustees of the McKnight Brain Research Foundation (MBRF) is to manage and to provide leadership to the Board of Trustees (Board). The Chair is accountable to the Board and acts as a direct liaison between the Board and the Executive Director (ED) to ensure that the Board's directives and resolutions are executed. The Chair acts as the chief communicator for the Board's decisions to the ED.

The duties and responsibilities of the Chair in relation to the Board are to:

Lead the Board to carry out its governance functions, ensuring the duties of care, obedience, loyalty and are fulfilled;

Ensure the Board approves and updates policies, including the MBRF Corporate Trust Agreement, for sound and compliant governance of the organization;

Ensure the ongoing recruitment, development, contributions and evaluations of Board members;

Manage the assessment of the performance of the Board and its committees, conduct evaluations of the Board, and make recommendations to the Board annually, regarding the effectiveness of the Board as a whole, as well as the Committees of the Board and individual Trustees;

Coordinate the strategic planning process through oversight of, direction to and partnership with the executive director;

Preside over regular and special meetings of the Board;

Review and sign minutes of all Board meetings;

Appoint, with Board approval, all committees, task forces and other special project roles of Board members in support of the organization's strategic plan;

Serve as ex-officio member of all committees of the Board;

Serve as an ambassador of the organization and advocate its mission to internal and external stakeholders;

Lead Board member development and succession planning.

Approved 11/8/2017

The duties and responsibilities of the Chair in relation to the ED are to:

Act as a liaison between management and the Board;

Serve as a trusted advisor to and provide independent counsel to the ED;

Partner with the ED to ensure the Board's directives, policies, and resolutions are carried out in a timely manner;

Ensure that the ED keeps the Board informed and that sufficient information is provided to enable the Board to develop appropriate decisions;

Establish priorities, and jointly create with the ED, the agendas for meetings of the Board;

Jointly with ED, serve as a spokesperson, when appropriate;

Jointly with ED, foster relationships with organizations and grant recipients;

Coordinate an annual performance review of the ED.

Qualifications of the Chair of the Board

Vision and capacity to inspire other volunteers;

Objectivity to hear all sides, listen well and manage a forum for input;

Extensive knowledge of the organization and its mission and impact;

Passion for the mission of the organization;

Ability to co-lead with a ED the strategic planning of the organization;

Ability to lead meetings through consent agendas, issues management and committee management;

Excellent communication skills with the ED, fellow Board members, grantees and other stakeholder audiences;

Ability to understand and manage with good humor, in partnership with the ED, the boundaries between the ED and Board Chair roles and responsibilities.

Duties of Vice Chair
Board of Trustees
McKnight Brain Research Foundation (MBRF)

1. **Substitute for Chair**

2. **Other tasks as assigned by the Chair or designated by the Board**

Approved: April 6, 2015

Chair Emeritus
McKnight Brain Research Foundation
Position Description

For J. Lee Dockery, MD
Founding Trustee and
First Chair Emeritus of the McKnight Brain Research Foundation

June 2019

Chair Emeritus is a title conveyed by the Board of Trustees of the McKnight Brain Research Foundation (MBRF) upon a former Chair of the Board of Trustees. The title is meant to achieve two goals: to recognize the individual's visionary leadership and extraordinary service while serving as Chair, and to convey upon this individual a new role with the MBRF. The Chair Emeritus title recognizes past exceptional achievement in advancing the mission of the MBRF while signaling the continued activities of the title holder in a more focused, yet equally important, role as it relates to the foundation's future success.

In April 2019, on the 20th Anniversary of his appointment as a founding Trustee, Dr. J. Lee Dockery was named the first Chair Emeritus of the McKnight Brain Research Foundation. Dr. Dockery is a valuable source of wisdom and institutional memory as well as continuing to hold forth a clear vision for the future of the MBRF and the field of research in cognitive aging, age-related cognitive decline and memory loss.

The Trustees of the MBRF feel strongly that Dr. Dockery's voice, ideas, and reputational standing are essential to continuing to address the vision and mission of the MBRF and the McKnight Brain Institutes (MBIs). Therefore, the Trustees extend an open invitation to Dr. Dockery to attend meetings of the Board of Trustees and to participate in any events of the MBRF and the McKnight Brain Institutes which he finds of interest.

The Trustees request that Dr. Dockery, within his availability and interest, assume the role and duties of ambassador, spokesman, and representative for the MBRF and that he will continue to foster current relationships and cultivate new relationships with partners and partner organizations on the foundation's behalf. Specifically, the Trustees request that Dr. Dockery attend the annual Inter-institutional Meeting of the McKnight Brain Institutes (if the meeting site is accessible to him); that he will continue to communicate with the Institute of Medicine (IOM) Working Group relative to the Report on Cognitive Aging; and that he attend or participate in other events, conferences, and meetings that his schedule, interest, and travel restrictions permit.

It is requested that Dr. Dockery participate as a member of the Membership and Governance Committee to help identify and recruit new Trustees and to offer insight into the committee's work related to governance. It is desired by the Trustees for Dr. Dockery to lead the Trustees' approved orientation program for all new trustees. It is also requested that Dr. Dockery lend his voice to the efforts of the Education Committee to seek inclusion of core competencies in cognitive aging in curricula and licensing requirements for Health Professionals. As spokesperson, Dr. Dockery may be called upon to work with the Communications Working Group to develop or review historical content, as well as to characterize and communicate the vision behind current activities and programs.

As Chair Emeritus, Dr. Dockery's performance of the duties outlined for the position is intended to be as selective and or comprehensive as compatible with his interest and availability. Dr. Dockery will be compensated at the same rate as the Trustees for his performance and participation in the activities described above, including reimbursement of Travel and related expenses benefitting the MBRF. The Chair Emeritus serves at the pleasure of the Board. The term is self-renewing and does not require renewal by the Board of Trustees.

Duties of the Corporate Trustee/Secretary for the McKnight Brain Research Foundation (MBRF)

1. Appointed as defined and authorized in the MBRF Trust Agreement;
2. Interact with Executive Director, Trustees and Board Chair, as necessary via print and electronic communications;
3. Interact with MBRF Executive Director, legal counsel and accounting representatives for tax preparation of the 990-PF, 990-T and 1099-MISC;
4. Interact with the personnel of the McKnight Brain Research Institutes, as directed by the MBRF Executive Director;
5. Manage all meeting arrangements, including securing meeting location, arranging for meals, arranging for telephones or audio visual equipment as necessary and making trustee reservations;
6. Travel to and attend Trustee meetings and site visits, as requested;
7. Prepare minutes of Trustee meetings for Executive Director review and submission to the Board Chair;
8. Serve as custodian and provide periodic reports to the Executive Director and Trustees on the inventory of the Foundation records, and maintain the archives for the historical records of the Foundation, located at the SunTrust offices, 333 S. Garland Avenue, 15th Floor, Orlando, FL 32801;
9. Act as a liaison between the portfolio managers of the Foundation and the Executive Director and legal counsel, for regular reports to the Trustees;
10. Handle capital calls for private equity holdings, and liquidation requests from equity fund managers approved by the portfolio manager;
11. Maintain accounts and disburse payments for the Travel Award Program, Bio-Informatics Core and Neuroimaging Core and Cognitive Aging Test Battery Working Group, and others as authorized by the Executive Director on behalf of the organization;
12. Handle deposits and payments for meeting venues and provide guidance as necessary to support the Executive Director in working with the host institution for the Inter-Institutional Meeting;
13. Handle payment of Trustee compensation, taxes, grant commitments, trustee expense reimbursements, travel award payments, Inter-Institutional meeting participant reimbursements, Executive Director travel reimbursements, and other expense reimbursements, as well as office operational expense payments as required;
14. Handle other Trustee or Executive Director hotel reservations and travel arrangements as necessary and requested by the Trustees and/or Executive Director
15. Perform other responsibilities assigned or delegated by the Board or Executive Director.

Approved November 8, 2017

McKNIGHT BRAIN
RESEARCH FOUNDATION
Preserving memory, enhancing life

POSITION SPECIFICATION
Executive Director
Remote
www.mcknightbrain.org

About the Opportunity

The new Executive Director (ED) will be a passionate, collaborative and driven professional who will serve as the chief administrative officer of the McKnight Brain Research Foundation (MBRF) and report directly to the Board of Trustees (Board) through the Chair of the Board. Along with the Chair, the ED serves as the lead representative of the organization and as the primary spokesperson for the MBRF.

The ED is responsible for overseeing all strategic planning, operations and administration of the organization's programs, finances, marketing and grant distributions. The ED serves as the organization's liaison to the Corporate Trustee, also overseeing the execution of the duties of the Corporate Trustee.

This is an exciting time to work at the forefront of brain research and to guide the Foundation in building awareness and helping better understand and alleviate the effects of age-related cognitive decline and memory loss.

More specifically, the Executive Director is charged with the following key responsibilities:

Organization Mission and Strategy

- Work with Board to ensure that the organization's mission is represented in its strategic planning goals;
- Implement and oversee grants to programs/organizations that carry out the organization's mission;
- Enhance MBRF's image by being active and visible in identified sectors and communities and by working closely with other professional, public and private organizations related to MBRF's mission;
- Ensure effective systems to track progress, regularly evaluate program components and communicate status of successes to the Board and other stakeholders;
- Build/expand partnerships, establish relationships with grantees, other funders of similar research and leaders at each grant site;
- Work with the Corporate Trustee and the personnel of the MBIs to ensure receipt of Annual Reports each year and distribute to the Trustees for review in a timely fashion;
- Work with the host institution of the annual Inter-Institutional Meeting to review contracts and, after approval by the Board, forward to Corporate Trustee for signature and payment of deposits and other costs related to the meeting;

- Create and implement programmatic strategy to better link and articulate the progress of the grantees in meeting the strategic goals of the MBRF.

Leadership & Management

- Ensure planning and implementation of strategic goals, and operational excellence in administration, finance, grant making and program evaluation, communications, and Board support, including all systems and resources needed to achieve those strategic goals;

- Actively engage and energize MBRF's Board members, grantees and other stakeholders;

- Report to and work closely with the Board to seek their involvement in policy decisions, and to increase the overall visibility of MBRF throughout the sector;

- Develop, maintain, and support a strong Board; serve as ex-officio of each committee; seek and build Board involvement with mission effectiveness;

- Regularly communicate with Board Chair and Trustees to provide updates and maintain an open line of communication;

- Serve as the primary liaison and oversee/manage the Corporate Trustee/Secretary relationship and interactions for the MBRF and Board;

- Establish and maintain relationships with various organizations throughout the brain/neuroscience research community, medical, clinical research and academic communities and utilize those relationships to strategically enhance MBRF's mission;

- Represent the Board and organization at meetings of professional organizations as deemed appropriate by the ED and/or Board;

- Represent the Board and organization at grantee site visits and meetings with other stakeholders;

- Establish employment and administrative policies and procedures for all day-to-day operations and functions of MBRF;

- Serve, along with the chair, as MBRF's primary spokesperson to the organization's constituents, media and the general public.

Board Governance

- Work with Board to fulfill the organization mission;

- Lead and represent MBRF in a manner that supports and guides the organization's mission as defined by the Board;

- Communicate effectively with the Board and provide, in a timely and accurate manner, all information necessary for the Board to function properly and to make informed decisions;

- In concert with the Board Chair, prepare the agenda for all Board meetings;

- Work with the Corporate Trustee to assemble and distribute Board agenda, support materials and information for Board meeting packages and upload those to Foundation's secure website;

- Review and edit minutes of the Board prepared by the Corporate Trustee, in concert with Board Chair, before the Corporate Trustee distributes minutes to the Board;

- As ex-officio member of each committee, in concert with the committee chairs, schedule meetings of the committees, develop the agenda, meeting materials and forward these items to the Corporate Trustee for uploading to the secure website;

- Review and edit minutes of all committee meetings prepared by the Corporate Trustee, in concert with Committee Chair, in advance of distributing minutes to respective Committees and the Board, as appropriate;

- Working with the Board Chair, annually ensure that Board members execute all annual personal policy forms (conflict of interest, document retention, travel, etc. as outlined in the Form – 990) for good governance and submit the record of completion of those to the Corporate Trustee.

Financial Performance

- Coordinate with the Corporate Trustee's preparation and submission of an annual operating budget to the Board; ensure preparation by the Corporate Trustee of quarterly financial statements, tax preparation of the 990-PF, 990-T and 1099-MISC, which accurately reflect the financial condition of the organization and its expenditures and investments;

- Responsible for fiscal management within the approved budget, ensuring maximum resource utilization, and maintenance of the organization in a positive financial position;

- Oversee and ensure the Corporate Trustee develops and submits regular performance reports from portfolio manager, and special reports as requested;

- Oversee and ensure the Corporate Trustee's execution of accounting and payment disbursal for all programs as authorized by the ED and Board;

- Oversee and ensure Corporate Trustee's execution of payment of trustee compensation, taxes, grant commitments, trustee and ED expense reimbursements, travel award payments, inter-institutional meeting participant reimbursement, other expense reimbursements, as well as operational expense invoices;

- Perform the final review of the Form 990 and other tax documents as prepared by the Corporate Trustee, before those are submitted to the Board for review and approval;

- Execute sound financial decision making for operating expenses.

Organizational Operations

- Effectively execute and administer MBRF's operations;

- With appropriate approvals, hire and manage competent, qualified staff and/or consultants; (Decision to hire approved via budget and functional approval of the board prior to hiring.)

- Sign all notes, agreements, grants, and other instruments made and entered into and on behalf of the organization. Board will predetermine all levels for approval;

Communications

- Handle all correspondence and requests for information regarding the affairs of the Foundation in a timely and professional manner;

- Deepen and refine all aspects of communications—from web presence, social media, and trade media to external relations with the goal of creating a stronger brand for MBRF;

- Maintain and regularly update communications vehicles, including the website and others to effectively communicate the Foundation's mission, grant investments, outcomes and benefits to society at large;

- Leverage external presence and relationships to garner new opportunities for collaborative funding and build national recognition for the importance of age-related cognitive decline and memory loss.

ABOUT THE SUCCESSFUL CANDIDATE

Professional Qualifications include:

- Ten or more years of senior management experience preferred or relevant comparable experience and background;
- Superior written and verbal communication skills, and public speaking skills;
- Strong marketing and public relations experience with the ability to engage a wide range of stakeholders through the use of a broad palate of communications strategies;
- Solid, hands-on, budget management skills, including budget preparation, analysis, decision-making and reporting;
- Strong organizational planning and delegation skills;
- Knowledge of grant making and grant monitoring unique to nonprofit sector;
- Demonstrated ability to oversee, collaborate and integrate the work of staff and consultants;
- Understanding of and/or experience in healthcare and/or academic environments;
- Knowledgeable and strongly supportive of the Mission and Purpose of the McKnight Brain Research Foundation (https://www.mcknightbrain.org);

Key Attributes include:

- Transparent and high integrity leadership;
- Ability to convey a vision of MBRF's strategic future to staff, Board, and other stakeholders;
- Persuasive and passionate communication skills with excellent interpersonal and multidisciplinary project skills;
- Skills to collaborate with and motivate Board members and other volunteers;
- Action-oriented, collegial, and adaptable approach to management;
- Ability to work effectively in collaboration with diverse groups of medical and research professionals;
- Passion, idealism, integrity, positive attitude, mission-driven, and self-directed;
- Ability to understand and manage in a professional and collegial manner;
- Ability to work in partnership with the Board Chair to identify and respect the boundaries between the Board Chair and ED's roles and responsibilities;

Education

- An advanced degree in either medicine, public health, nursing, basic and life sciences, business or liberal arts and sciences from a recognized university accredited through the US Department of Education and the Council on Higher Education;
- A master's degree or equivalent is the minimum requirement for consideration.

Travel

- Ability to travel 6-8 days per year to attend Trustee meetings and the annual Inter-Institutional Meeting in person.

About the McKnight Brain Research Foundation

Founded in 1999 by Evelyn F. McKnight, the McKnight Brain Research Foundation is the only private foundation devoted exclusively to solving the mysteries of the aging brain and helping people achieve a lifetime of cognitive health. With cognitive changes due to the normal aging process potentially affecting up to 87 percent of people age 65 and older, the McKnight Brain Research Foundation works to champion research to better understand age-related cognitive decline and memory loss. As leaders in cognitive aging research, the Foundation is also committed to sharing its research findings and practical suggestions for maintaining brain health with the public.

Since its founding, the Foundation has established Evelyn F. McKnight Brain Institutes at the University of Alabama at Birmingham, the University of Arizona, and the University of Miami, and the Evelyn F. and William L. McKnight Brain Institute at the University of Florida.

By partnering with the Foundation for the National Institutes of Health, and with the support of three Cognitive Aging Summits and the National Academy of Medicine Cognitive Aging Report, the McKnight Brain Research Foundation has made great progress toward better understanding the effects of age-related cognitive decline and memory loss over the last two decades and will continue promoting growth of the field through scholarships, research awards and programs.

COMPENSATION

Salary is competitive and commensurate with experience.

The McKnight Brain Research Foundation is an Equal Opportunity Employer and encourages candidates of all backgrounds to apply for this position.

Please email cover letter and resume or nominations in confidence to:
Melanie.Cianciotto@truist.com by Sunday, May 15, 2022.

Angelika Schlanger, PHD

Executive Director, McKnight Brain Research Foundation

Dr. Angelika Schlanger is a strategic, authentic, and vision-driven leader dedicated to transforming communities through the power of philanthropy and social impact. Dr. Schlanger has cultivated a unique blend of skills and lived experiences culled from two decades of academic, government, nonprofit, and corporate leadership positions. She has driven over $100M in philanthropic investments across 500+ grants in multiple program areas, sectors, and geographic regions, impacting the lives of over a million adults and children to date.

Dr. Schlanger previously served as the Director of The Frederick A. DeLuca Foundation, one of the country's largest family foundations. As its leader, Dr. Schlanger was instrumental in transforming the foundation from a relatively unknown entity in Florida into a driving force for collaborative impact. During her tenure, Dr. Schlanger rapidly scaled the Foundation, built an infrastructure and strategic grantmaking program, and cultivated powerful partnerships across nonprofits, community leaders and experts. Her leadership positioned The Frederick A. DeLuca Foundation as one of the most trusted and well-recognized philanthropic institutions in the South Florida region, garnering the Outstanding Foundation Award (2019) in Broward County, amongst other accolades.

Prior to joining The Frederick A. DeLuca Foundation, Dr. Schlanger served as a Regional Public Health Specialist for the University of Florida/IFAS Extension Family Nutrition Program across five counties. In this role, she coordinated community initiatives, developed collaborations, and drove school-based strategies to increase access to healthy foods, nutrition education and physical activity for low-income youth and families. Her impact involved the development of school board wellness policies in four school districts, including the 6th and 10th largest school districts in the nation.

Dr. Schlanger currently serves as the Executive Director of the McKnight Brain Research Foundation, where she collaborates with the Board of Trustees to lead initiatives, grantmaking programs, and partnerships that advance research and educational outreach around brain health and cognitive aging.

Dr. Schlanger received her B.A. from the University of Pennsylvania with Honors in French and History; a Masters from Columbia University in Political Science; and a Ph.D. in Political Science, with Distinction, from Yale University. Dr. Schlanger is a devoted basketball coach, youth mentor, community advocate, and mom to three wonderful children. She recently received the "Prestigious Women Award" as a Nonprofit Executive from South Florida Business and Wealth.

Executive Director Goals for 2022-2023

Executive Director Name	Revised and Approved by the Executive Committee
Angelika Schlanger	**May 2023**

1. Organizational Goals		
Area	**2022-23 Goals to be Reviewed and Approved July/August 2023**	**Results to be Reported June 2023**
Board Development, Membership and Governance	Develop positive and productive relationship with all the Trustees through introductory calls and continued engagement Advance the candidate nomination and recruitment process to add at least two new Trustees to the board in 2023 Develop regular meeting cadence with MBRF Chair to share updates and receive ongoing feedback Proactively schedule committee meetings when appropriate and develop relevant meeting materials	
McKnight Brain Institute Relations	Develop collaborative relationships with the MBIs and work to understand the unique structure & history of each MBI Work with MBIs to support their efforts to seek wider participation in the pilot grant program and enhance awareness of this initiative within MBIs	

	Participate and support the Communications Working Group to ensure consistent meeting schedule and continued collaboration between the communications representatives of the MBIs and the MBRF	
External Partner Relations	Continue to nurture current external partner relationships, understanding the unique history, and shared goals Identify national collaborative networks to engage with other like-minded organizations and increase visibility of the mission and strategic initiatives of the MBRF Identify potential new partners for promotion of MBRF messages and distribution of educational resources Grow the MBRF's network of like-minded organizations and funders to explore synergies and share learnings	
Strategic Development - Education	Develop and implement national search process to identify a consulting firm to complete a landscape analysis and scoping document for the PCP Initiative Work with the consultant to ensure successful completion of the study Develop and share strategic recommendations to the board on how to advance the PCP initiative, based on the completed study Begin implementing board-approved strategy/strategies for the PCP initiative	

Strategic Development - Communications	Implement all components of current communications plan Develop cadence of quarterly tracking and reporting to Trustees on key metrics (web site traffic, social media engagement, etc.) Lead process to develop new communications plan and proposed budget starting July 2023 Continue to highlight the MBI and MBRF activities, events, news and activities on social media and website Increase development of new content for the website that will attract and engage more visitors to McKnightBrain.org Increase audience engagement with MBRF web site, newsletter and social media channels	
Strategic Development – Research	Continue to work closely with funding partners on current research partnerships, programs, scholarships and awards Continue to work with awardees to follow and track progress and outcome(s) Work with research scholarship partners to increase number of applications Strive to improve the review and award process, working with Trustees and partners (ABF and AFAR) Initiate planning and partnership with NIA/FNIH for Cognitive Aging Summit IV	

Finance and Administrative Operations	Continue to monitor with the Corporate Trustee the operations expenses against the current operating budget Continue to monitor funding for the communications plan and related special activities and promotions Monitor budget for Education Landscape Analysis Initiative Continue to monitor with the Corporate Trustee all grant timelines, reports, and expenses Ensure grantee reports are submitted on a timely basis and are reviewed by the Trustees Support the Corporate Trustee and the Trustees in their review of financial and investment reports	

2. Demonstrating Performance Factors to be Completed in July 2023

To what degree did you, the Executive Director, demonstrate the following personal attributes, leadership qualities, and competencies in the past year?

Personal Attribute or Leadership Quality	Action that demonstrates Attribute or Quality	Rating 1 - 4
Serves as Change Agent		
Problem Solving		
Systems Thinking		
Partnership Focus		
Effective Communication		

Ethics and Judgment		

Core Competencies	Action that demonstrates Competency	Rating 1 - 4
Understanding of Nonprofit Governance and Management		
Focus on MBRF Key Priorities and Functions		
Understanding of the MBIs' Structure, Research Focus, and Current Priorities and Needs		
Program Management and Oversight		
Ability to See Opportunity and Assess Risk		

Comments: In what priority areas of performance did you, the Executive Director, excel? In what areas is greater emphasis or more action or effort needed?

3. Summary Assessment for August 2022- August 2023, Next Steps, and Vision for the Organization

Overall performance rating: _____

4 - Exceeds Expectations
3 - Meets Expectations
2 - Partially Meets Expectations
1 – Requires Increase in Emphasis or Effort

Comments to be provided by the Board of Trustees

1. What are 1-3 notable areas of the Executive Director's strength?

2. What are 1-3 areas for greater emphasis and understanding or an increase in activity?

3. What do you see as your vision for the MBRF in the next year? Is your vision reflected in the goals set forward by the Executive Director? If not, please note here.

4. Board Self-Reflection

1. What have you, the Trustees as a whole, done well or effectively to provide support to the Executive Director?

2. What might the Trustees have done differently?

3. As you review the goals for next year, what support is needed from the Trustees to move each area of accountability forward?

4. What goals would you establish for the Board of Trustees for next year?

Board of Trustees
Reorganization Summary
And
MBRF Priority Areas

Board of Trustees Reorganization Summary
And Priorities for 2020 – 2023

Since its inception in 1999, the McKnight Brain Research Foundation (MBRF) was managed by consensus of the three founding trustees. Founding Trustee, Dr. Lee Dockery, served as the primary coordinator and manager. However, upon the establishment of the four McKnight Brain Institutes, the trustees felt the need for additional assistance in reviewing progress and making site visits. A fourth trustee was added in 2006 and a fifth in 2009. Currently there are six trustees in addition to the Coprorate Trustee and Chair Emeritus serving. A maximum of eleven trustees are allowed in the MBRF's Trust documents.

The duties and responsibilities of each trustee were developed and approved in 2015. A Chair and Vice Chair were elected in 2015. At the strategic planning meeting in 2017, it was reaffirmed by the trustees that the MBRF would continue in perpetuity. In doing so, the MBRF committed to becoming a more public-facing organization. With Dr. Lee Dockery's announcement of his intention to retire in 2019, the trustees voted establish a part-time Executive Director position who would become the Chief Administrative Officer of the MBRF. After a successful national search, Amy Porter accepted the offer and became the first Executive Director in April 2018.

With the impending retirement of Dr. Lee Dockery as MBRF Chair, the trustees recognized the need for enhanced individual and collective participation by the trustees. The justification and plan for reorganization were approved by the Board of Trustees at its meeting on October 30, 2018. The approved reorganization plan created an operational board structure composed of the Chair, Vice Chair, the Chairs of five new standing committees, the Executive Director, Corporate Trustee and the Chair Emeritus.

The five approved standing committees are:

1. Communications
2. Education
3. Finance
4. Membership and Governance
5. Research

As an outcome of the reorganization of the Board of Trustees, programs in Communications, Educations and Research were identified as priority areas of growth and development by the MBRF for 2020-2023.

The charters for each of the committees were approved by the Board of Trustees on February 20, 2019, and are included for review and information. The list of members of the committees is also included. It is hoped that each MBRF Trustee participates on at least two committees upon invitation by the MBRF Chair.

Included in the charters of the Communications, Education, and Research Committees are provisions for non-trustee advisory members to be appointed to those three committees. The advisory members provide expertise in committee priority areas. Criteria for appointment of advisory members is included in this section.

With the establishment of standing committees, the MBRF is able to assign responsibility for implementation and oversight of the three priority programs.

1. Communications Committee
   Chair: Richard I Isaacson, MD
   Purpose and Powers: See Charter

A. Summary of Activity

- Appointed Valerie Patmintra Senior Communications Advisor (Bio attached).
- Convened Communications Working Group meeting.
  (See Attached Charter and Working Group Membership Attached).
- A two-year communications plan with a budget not to exceed $300,000
  (See attached prospectus).
- Endorsed Key Messages statement on cognitive aging, Cognitive Decline, and Memory Loss developed by the communication working group. (See Attached).
- Produced a short video commemoration of the 20-year history of the MBRF and was shown at the April 10, 2019, Inter- institutional Meeting. The video resides on the MBRF website.
- First Communications Workshop was held in connection with the 11th Inter-Institutional meeting (April featuring a panel discussion on the importance of Communication of the science surrounding age related cognitive decline and memory loss.
- The newly developed and redesigned MBRF website was launched including individual MBI website content and links to between each other of the individual MBI websites.
- Trustees previewed first draft of MBRF/MBI organizational brochure describing the organizational relationship between the MBRF and each of the MBIs as well as individual profiles of each MBI.
- Approval of a link from the MBRF website to MindCrowd website. MindCrowd is a web-based memory study designed to analyze how genetics influences memory. Participants age 18 or older are invited to take a 10-minute online test. It was thought individuals visiting the MBRF website would benefit from the additional information on age-related cognitive decline and memory loss on the MindCrowd website and could contribute to the research finding by taking the examination. For more information, visit www.mindcrowd.org.
- Developed a social media initiative through Twitter and LinkedIn to share info from MBRF and the MBIs. Articles and events are posted to the Twitter feed regularly. The new MBRF logo is in use on Twitter.

B. Goals for 2020-2021

- Continue to buildout website and content development development.
- Continue development of organizational brochure.
- Produce and upload organizational brochure.
- Continue to grow the collaborative relationship with the MBIs through the communications working group.

- **<u>Board Approved Priority</u> -- Proceed with efforts to build the audience for the MBRF website and social media platforms. Develop strategies to reach Primary Care Physicians (PCPs) as a target audience. (Audience Building Plan included with this document.)**

2. Education Committee
   Chair: Robert Wah, MD
   Purpose and Powers: See Charter

A. Summary of Activity

The Education Committee (with the Research Committee) reviews content before it is posted on website, published, or included in print materials or slide presentations, ensuring consistency with key messages. The committee reviews for accuracy, soundness, and alignment with the MBRF mission, current scientific understanding, and clinical practice.

- Develop and curate website content addressed to individuals, families and caregivers of those with age-related cognitive decline and memory loss.
- Develop and curate website content developed for individuals on how to protect, maintain brain health.
- Develop brochure copy to raise awareness and promote the MBIs and MBRF to individuals, partners, donors.
- The Annual Inter-Institutional Meeting between the four MBIs has served to identify educational opportunities and implement activities inspiring commitment and shared vision.
  The 12th Inter-institutional meeting scheduled for April 2020 was cancelled due to the pandemic and has been rescheduled for April 2021, although this date may be adjusted to the fall of 2021.
- The McKnight Scholars will be invited to the 2021 Inter-Institutional Meeting to meet the researchers at the MBIs and for the graduating scholars to present on their research.
- The Annual William G. Luttge Annual Lectureship in Neuroscience at the University of Florida is presented by a research scientist of national or international prestige in the field of neurosciences. The Lectureship was established in 2012, honoring the Founding Director of the Evelyn F. and William L. McKnight Brain Institute at the University of Florida. Lectureship value--$250,000; Expense Fund--$50,000 for immediate inauguration of the Lectureship.

- **<u>Board Approved Priority</u> – Identify, develop, and disseminate educational content for Primary Care Physicians (PCPs) as a much-needed resource in their practices. (See PCP Content Outline included with this document.)**

3. Research Committee
   Chair: Madhav Thambisetty, MD, PhD.
   Purpose and Powers: See attached Charter
   A. Summary of Activity
   - Appointed Dr. Robert Krikorian as the first advisory member to a committee after the reorganization of the Board of Trustees in October 2018. Dr. Kirkorian is Professor of Psychiatry and Behavioral Neuroscience at the University of Cincinnati Health Center.
   - Reviewed and revised, in collaboration with the finance committee, the template for the MBI Annual Report to the MBRF to make it easier to read and evaluate.
   - Approved a request from the MBI at UM for $200,000 for pilot funding over two years to establish a Neurocognitive Post-Doctoral Clinical Fellowship to begin July 1, 2020.
   - Approved a request from the MBI at UA for $244,400 for participation in the Precision Aging Demonstration Pilot by its partner MBI at UM to provide additional cohort sample data requested by the NIH following preliminary review.
   - Reviewed and approved two Inter-Institutional grant proposals recommended for funding by the Cognitive Aging and Memory Intervention Core Committee.

     1. Vulnerability of Older Adults to Financial Deception Schemes—A Novel Intervention Tool--$60,000 per year for two years.

     2. A pilot Intervention with Near Infrared Stimulation: Revitalizing Cognition in Older Adults. --$60,000 per year for two years.

     3. Transcutaneous Vagal Nerve Stimulation and Cognitive Training $60,000 per year for two years.

- Reviewed and recommended renewal of the Research Partnership in Cognitive Aging with the National Institute of Aging (NIA) through the Foundation for NIH for the third five-year cycle to begin in Spring of 2020 (Postponed until Spring 2021), (1st cycle-2009, 2nd cycle 2014, 3rd cycle approved 2019). It is expected the MBRF will fund $1 million per year for five years and will be matched by the NIA at $2 million year for five years.
- Approved the request to fund the Reserve & Resilience Workshop Pilot Grants Project for 2020. The MBRF supported the 2019 workshop for $30,000 at which there were over 300 Attendees (8 MBI researchers). The National Workshop on Cognitive Reserve and Resilience is an outcome of Cognitive Aging Summit III funded by the MBRF with the NIA through the FNIH.
- Reviewed and recommended for funding two McKnight Brain Research Foundation Clinical Translational Research Scholarships through the American Academy of Neurology (AAN) and American Brain Foundation (ABF). Each scholarship award is for $150,000 for the two-year period. The 2020 McKnight Scholars is third cycle of for the scholarships.
- The MBRF hosts an Annual Poster Reception in conjunction with the Annual Meeting of Society for Neuroscience (SfN). The annual meeting scheduled for October 24 – 28, 2020 was cancelled. The 2019 Poster Reception had 70 posters submitted and were judged By Dr. Molly Wagster and Dr. Jon King from the NIA. Cash awards were made for 1st, 2nd and 3rd place plus three honorable mention awards.
- In collaboration with the education committee, approved Content Outline for PCPs' area of the McKnightBrain.org Website and resources to be added to the McKnightBrain.org website to support the educational initiative targeting PCPs. (See attached Content Outline for PCPs).
- In collaboration with the communication, education committees, approval of a link from the MBRF website to MindCrowd website., MindCrowd is a web-based memory study designed to analyze how genetics influences memory. It was thought individuals visiting the MBRF website would benefit from the additional information on age related cognitive decline and memory loss on the MindCrowd Website and could contribute to the research finding by taking the examination. For more information, visit www.mindcrowd.org.

- **<u>Board Approved Priority</u> - The Research Committee developed a proposal to establish the McKnight Brain Research Foundation Mid-Career Research Award in Cognitive Aging and Memory Loss with the following commitments:**
  - **a. Length of award: three years, renewal annually after satisfactory review.**
  - **b. Amount of Award: $250,000 per year with match from the host institution.**
  - **c. The Foundation commits to funding the program for a five-year initial trial period which would have supported 12 scientists at the conclusion of the five-year cycle.**

  The Research Committee developed a prospectus describing the McKnight Brain Research Foundation Mid-Career Research Award in Cognitive Aging and Memory Loss suitable to distribute to potential partners to jointly sponsor and fund the mid- career research awards. (See Prospectus).

McKnight Brain Research Foundation

Charter of the Membership and Governance Committee

of the Board of Trustees

Purpose

The Membership and Governance Committee shall coordinate the Board of Trustees' oversight responsibilities by periodically reviewing Board composition and by identifying, recruiting, and recommending candidates for appointment, or re-election of current Trustees, consistent with applicable qualifications required by the April 6, 2015, document "Board Member Duties and Responsibilities." The Committee shall review periodically, or as requested by the Chair of the Board, the succession process for officers of the Board. The Committee shall oversee annual board self-evaluations, Trustee orientation and training, and will periodically review and make recommendations on Board size, committee structure, charters, policies, process, and practices of the Board and its Committees. The Committee shall recommend to the Board the establishment of special committees and advisory councils. The Membership and Governance Committee reports to the Board of Trustees.

Members

The Chair of the McKnight Brain Research Foundation (MBRF) Board of Trustees shall appoint a Membership and Governance Committee, consisting of no fewer than two (2) members, inclusive of the Chair of the Committee. The Chair of the Board of Trustees shall serve as non-voting, ex officio member. The Executive Director shall serve as a non-voting, ex officio member. All members shall be MBRF Trustees.

Meetings

The Membership and Governance Committee shall meet at those times and places as determined by the Chairman of the Membership and Governance Committee, no fewer than two (2) times a year. The Committee shall maintain minutes of all meetings, which shall be regularly approved by the Committee and made available for distribution to the Board of Trustees.

Powers

The Committee shall recommend to the Board of Trustees candidates for appointment and re-election as Trustees. These candidates shall demonstrate knowledge, passion and commitment to the mission of the McKnight Brain Research Foundation, as well as sound judgment and a willingness to act collaboratively. The Committee shall periodically review Board composition for the appropriate balance of expertise, specialty, size, structure, and diversity and make recommendations to the Board of Trustees. The Committee shall develop orientation material and participate in the orientation and training of new Trustees. The Committee shall review Trustee self-assessment tools and make recommendations to encourage 100% participation. The Committee shall periodically review the charters of all Board Committees and recommend to the Board of Trustees any changes and additional committees or advisory councils to be established. The Committee shall perform such other duties as may from time to time be required by the Board of Trustees.

Approved by the Board of Trustees on February 20, 2019

McKnight Brain Research Foundation

Charter of the Finance Committee

of the Board of Trustees

Purpose

The Finance Committee shall coordinate the Board of Trustees' financial oversight responsibilities. The Committee shall be responsible for the planning, monitoring, and evaluation of the McKnight Brain Research Foundation's (MBRF) policies and programs for funding, financial management, assets, risks, and insurance. The Finance Committee reports to the Board of Trustees.

Members

The Chair of the McKnight Brain Research Foundation Board of Trustees shall appoint a Finance Committee, consisting of no fewer than three (3) members, inclusive of the Corporate Trustee, and the Chair of the Finance Committee, and at least one (1) other Trustee. The Chair of the Board of Trustees shall serve as non-voting, ex officio member. The Executive Director shall serve as a non-voting, ex officio member.

Meetings

The Finance Committee shall meet at those times and places as determined by the Chair of the Finance Committee, no fewer than two (2) times a year. The Committee shall maintain minutes of all meetings, which shall be regularly approved by the Committee and made available for distribution to the Board of Trustees.

Powers

The Finance Committee monitors MBRF's financial records; reviews and oversees the creation of accurate, timely, and meaningful financial statements to be presented to the Board of Trustees; reviews annual MBRF operating expenses; reviews financial reporting from McKnight Brain Institutes (MBIs); anticipates financial risks; monitors and ensures safeguarding of MBRF assets; monitors compliance with federal, state, and other financial reporting requirements; ensures adequacy of MBRF internal controls and compliance with conflicts of interest policy and other code of conduct policies; and advises the Trustees on the status of the MBRF's finances, and those reported by the MBIs. The Finance Committee works with the Corporate Trustee, the Investment Manager, the Chair of the Board of Trustees, and the Executive Director to develop long range financial planning. The Committee shall perform such other duties as may from time to time be required by the Board of Trustees.

Approved by the Board of Trustees on February 20, 2019

McKnight Brain Research Foundation

Charter of the Communications Committee

of the Board of Trustees

Purpose

The Communications Committee shall provide strategic direction to the communications programs to ensure effective communication of the McKnight Brain Research Foundation's (MBRF) mission, initiatives, and programs, and to evaluate the effectiveness of strategies for raising the profile of the MBRF and the McKnight Brain Institutes (MBIs). The Communications Committee shall identify opportunities and implement activities to foster greater public awareness of cognitive aging and age-related cognitive decline and age-related memory loss (which are distinct from pathologic disease states, such as Alzheimer's disease and related dementias.) The Communications Committee reports to the Board of Trustees.

Members

The Chair of the Board shall appoint a Communications Committee, consisting of no fewer than three (3) members, inclusive of the Chair of the Communications Committee and at least two other Trustees. The Chairman of the Board shall serve as non-voting, ex officio member. The Committee may include other non-Trustee persons whose experience in social media, public relations, publications, marketing, and may assist the Committee and the Board of Trustees in the role of spokespersons. The Executive Director shall serve as non-voting, ex officio member.

Meetings

The Communications Committee shall meet at those times and places as determined by the Chair of the Committee, no fewer than two (2) times a year. The Committee shall maintain minutes of all meetings, which shall be regularly approved by the Committee and made available for distribution to the Board of Trustees.

Powers

The Communications Committee shall provide oversight and guidance on the communications activities promoting the work of the MBRF, inclusive of its partnerships, educational programs and scientific research. The Committee shall provide oversight on reaching the goals of the approved Communications Plan, review and approve development of future Communications Plans, as well as branding strategies, national awareness campaigns, website development and maintenance, and social media strategies developed by the MBRF. The Committee will seek information and recommendations from the MBRF/MBI Communications Working Group (an inter-institutional group) to promote activities and research at the McKnight Brain Institutes, attendance at inter-institutional meetings and events, and generate interest in scholarship and core grant opportunities. The Communications Committee will periodically review the goals, strategies, marketing plans, and implementation of communications efforts. The Committee will monitor progress on the communications plan and timeline, and will advise the Trustees on the progress to date and make recommendations and request Trustee involvement.

The Communications Committee shall work with the Chair of the Board of Trustees and the Executive Director to develop future Communications Plans and Timelines, and shall perform such other duties as may from time to time be required and approved by the Board of Trustees.

Approved by the Board of Trustees on February 20, 2019

McKnight Brain Research Foundation

Charter of the Education Committee

of the Board of Trustees

Purpose

The Education Committee shall lead efforts to inform the public, the scientific community, health policy agencies, health professional schools, professional societies, and the media on the prevalence and impact of age-related cognitive decline and memory loss, differentiating this natural process from Alzheimer's disease and other dementias.

The Committee shall develop information and resources to assist those living with cognitive decline and age-related memory loss and their family members to better understand, address, and manage cognitive changes and the effect and impact on their lives. The Education Committee shall develop and disseminate information to the public on activities and behaviors that can maintain cognitive health throughout life and help delay or minimize the negative effects of cognitive aging.

The Education Committee shall identify educational opportunities and implement activities among the scientific community to foster greater interest and investment, and to inspire commitment and shared vision in the understanding and alleviation of cognitive aging and age-related cognitive decline and memory loss. The Education Committee shall encourage and endorse educational programs at each of the McKnight Brain Institutes (MBIs) by providing direction, focus and guidance using consistent information and key messages on cognitive aging, age-related cognitive decline and age-related memory loss.

The Education Committee shall work to elevate the importance of age-related cognitive decline and memory loss on the national agenda and shall encourage its inclusion in health professional education curricula, accreditation, examination, and licensing, as well as encouraging greater investment in research and education by federal health agencies. The Education Committee reports to the Board of Trustees.

Members

The Chair of the Board shall appoint an Education Committee, consisting of no fewer than three (3) members, inclusive of the Chair of the Education Committee and at least two other Trustees. Because the Committee is required to make substantive judgments about the content and quality of educational programs, targeting a varied audience and utilizing a variety of delivery methods, the committee may include other non-Trustee members. The Chair of the Board shall serve as non-voting, ex officio member. The Executive Director shall serve as non-voting, ex officio member.

Meetings

The Education Committee shall meet at those times and places as determined by the Chair of the Committee, no fewer than two (2) times a year. The Committee shall maintain minutes of all meetings, which shall be regularly approved by the Committee and made available for distribution to the Board of Trustees.

Approved by the Board of Trustees on February 20, 2019

Powers

The Education Committee shall provide oversight and guidance on education activities, inclusive of its partnerships and programs, and assist in plans for the annual Inter-institutional meeting. The Committee shall review and approve all educational materials distributed under the auspices of the MBRF.

The Committee shall share information about scholarship opportunities, panel and presentation opportunities, poster sessions, conference participation, and educational partnerships with nonprofit organizations and health policy agencies and encourage McKnight Brain Research Foundation (MBRF) Trustee and MBI participation.

The Education Committee shall encourage health professional schools, professional societies, and public and private health care organizations to develop and disseminate core competencies, curricula, and continuing education opportunities that focus on cognitive aging as distinct from clinical syndromes and diseases. The Committee shall encourage that cognitive health should be promoted during regular medical and wellness visits for people of all ages.

The Education Committee shall work with the Chair of the Board of Trustees and the Executive Director to develop long range plans, and shall perform such other duties as may from time to time be required and approved by the Board of Trustees.

McKnight Brain Research Foundation

Charter of the Research Committee

of the Board of Trustees

Purpose

The Research Committee shall encourage and assess research at the McKnight Brain Institutes (MBIs) by providing direction, focus and guidance for research that supports the McKnight Brain Research Foundation's (MBRF) mission to investigate cognitive aging, age-related cognitive decline and age-related memory loss (unrelated to Alzheimer's disease or other dementias). The Research Committee shall identify opportunities to promote and implement activities among the scientific community to foster greater interest in cognitive aging and age-related cognitive decline and memory loss. The Committee, by their example and leadership, shall encourage young investigators in this area of research. The Research Committee reports to the Board of Trustees.

Members

The Chair of the Board shall appoint a Research Committee, consisting of no fewer than three (3) members, inclusive of the Chair of the Research Committee and at least two other Trustees. Because the Committee is required to make substantive judgments about the quality of research studies and protocols, familiarity with research is the single most important criterion for service on the committee. The Chair of the Board shall serve as non-voting, ex officio member. The Committee may include other non-Trustee persons. The Executive Director shall serve as non-voting, ex officio member.

Meetings

The Research Committee shall meet at those times and places as determined by the Chair of the Committee, no fewer than two (2) times a year. The Committee shall maintain minutes of all meetings, which shall be regularly approved by the Committee and made available for distribution to the Board of Trustees.

Powers

The Research Committee shall provide oversight and guidance on research activities, inclusive of its partnerships and programs. The Research Committee shall review all requests, proposals and applications for funding of research or scholarships. The Research Committee makes recommendations on the merits and limitations of these requests to the MBRF Board of Trustees and may offer adjustments to the study protocol to allow for alignment with the MBRF mission. The Committee shall review and approve for recommendation the objectives and methods of study designs. The Committee will seek information and recommendations from the Cognitive Aging and Memory Interventional Core Committee and the MBRF Leadership Council and MBI Directors. The Committee will monitor progress on funded research studies, and will advise the Trustees and make recommendations.

The Research Committee shall work with the Chair of the Board of Trustees and the Executive Director to develop long range plans, and shall perform such other duties as may from time to time be required and approved by the Board of Trustees.

Approved by the Board of Trustees on February 20, 2019

McKnight Brain Research Foundation
Board of Trustees
Committees and Members

July 2023

Membership and Governance Committee

Susan L. Pekarske, MD, Chair
Melanie A. Cianciotto
J. Lee Dockery, MD
Michael L. Dockery, MD
Madhav Thambisetty, MD, PhD

Finance Committee

Allison Brashear, MD, MBA, Chair
Melanie A. Cianciotto
Michael L. Dockery, MD
Susan L. Pekarske, MD

Communications Committee

Patricia Boyle, PhD, Chair
John Brady, MD
Sharon A. Brangman, MD, FACP, AGSF - *tentative*
Michael L. Dockery, MD
Susan L. Pekarske, MD

Education Committee

John Brady, MD, Chair
Patricia Boyle, PhD
Allison Brashear, MD, MBA
Sharon A. Brangman, MD, FACP, AGSF - *tentative*
Roy H. Hamilton, MD, MS, FAAN, FANA, FCPP - *tentative*
Michael L. Dockery, MD

Research Committee

Madhav Thambisetty, MD, PhD, Chair
Patricia Boyle, PhD
Michael L. Dockery, MD
Roy H. Hamilton, MD, MS, FAAN, FANA, FCPP - *tentative*
Susan L. Pekarske, MD

McKnight Brain Research Foundation
Qualifications for Advisory Committee Members

1. The Board of Trustees of the McKnight Brain Research Foundation (MBRF) has approved non-trustee appointments for membership on three (3) of the MBRF board committees. These committees are the Communications Committee, the Education Committee, and the Research Committee.

2. Trustees serving on committees shall be referred to as "Trustee Members." Non-trustee members of committees shall be referred to as "Advisory Members." Advisory Members serve in a volunteer capacity and receive no compensation.

3. Advisory Members will support the Mission and Purpose of the MBRF by having the experience, education and qualifications to advance the specific goals and activities of the Committee to which they are appointed.

4. Advisory Members are appointed by the Committee Chair. Members serve one (1) year terms, renewable three (3) times, at the Chair's discretion. Advisory Members may serve on more than one (1) Committee, or may be appointed to another Committee at the end of her or his term.

5. An Advisory Member may be invited by the Board of Trustees to attend MBRF meetings, conferences, and events. Invitations will be extended from the Chair of the Board of Trustees. Travel and other expenses related to attending will be reimbursed.

6. Advisory Members must be committed to the Values, Vision, Mission and Code of Ethics of the McKnight Brain Research Foundation.

MBRF Program Priority Areas
2020 – 2023

Communications – Audience Building Plan

Education –Outline of Primary Care Physician Content for mcknightbrain.org

Research – Mid-Career Research Award in Cognitive Aging and Memory Loss

McKnightBrain.org Audience Building Plan

I. Attracting General Site Visitors

- **Blogging/Guest Blogging**
  - Adding a blog feature to the website with monthly blogs posted by MBRF Board members, MBI scientists and experts from partner organizations will help boost search results and keep the site fresh with new content
  - Blogs can be tied to new research, current events or commenting on outside science and research to keep ideas fresh each month
  - Guest blogging on partner organization and medical magazine sites can help attract new audiences and drive traffic back to McKnightBrain.org

- **Key Words and Search Engine Optimization**
  - **Build relevancy:** Analyze common words people search for in the field – from general terms like brain health to specific terms and phrases like age-related memory loss and cognitive decline and make sure the site is optimized to use these terms consistently. When site content matches what people search for, it boosts relevancy and increases presence across search engines.
  - **Become an Authority:** The more other sites link to McKnightBrain.org will also help build a presence on Google and other search engines. Look for opportunities where partner organizations can link back to McKnightBrain.org as the authority on age-related memory loss and cognitive decline. Make sure McKnightBrain.org is featured on and linked from all of the MBI websites, reach out to FNIH, NIH, NIA and other partner groups letting them know about the new site and asking for links to our content as appropriate.

- **Build a Social Presence**
  - Leverage Facebook and Twitter to share curated content and drive traffic consistently back to McKnightBrain.org
  - Create a monthly content calendar of posts to share site content, tips and advice, as well as news and information from the MBIs and other partner organizations
  - Link posts back to the website

- **Paid Digital Advertising**
  - **Run a paid Google search ad campaign:** Identify key words and set a budget to reach a daily maximum spend based on clicks or set a max spend for the life of the campaign. With Google, you only pay for clicks through to the website and ads appear when people search for the key words we select.
  - **Facebook ads:** Using a single image or short video clip, you can create Facebook ads to help build an audience for the website as well as build followers on Facebook. With highly customizable demographics, you can target people with specific interests or by age, sex, etc. to increase social and website engagement.

- **Display advertising:** Create visual banner ads to appear on other sites based on individual's interests.
- **Email Marketing:** Purchase targeted email lists and send newsletters, seasonal emails, and/or emails to announce events, awards, scholarship opportunities with links driving back to the website.

II. Leveraging New Awards Program and Primary Care Physician Content to Attract Targeted Audiences

1. Announcing and Driving Traffic to the New Mid-Career Research Awards Program

- **Leverage Social Networks**
  - Draft scheduled social media posts announcing award program, highlighting key dates, profiling awardees and encouraging applications
  - Launch a Facebook ad campaign targeting midcareer researchers – campaign budget can be set to reach a set number of people per day or for the lifetime of the campaign (for example, one month leading up to the application deadline)

- **Activate Partner Organizations**
  - Share social media posts with MBIs and other partners, encouraging them to post and share with their networks
  - Develop web banners MBIs and other partners can post to their websites linking to the award information on the MBRF website
  - Purchase banner/e-Table of Contents ads in partner publications and relevant journals targeting mid career researchers

2. Announcing and Promoting the New PCP Resources

- **Leverage Social Networks**
  - Draft scheduled social media posts highlighting the importance of talking with older adults about cognitive health and driving back to specific resources for PCPs
  - Launch a Facebook ad campaign targeting primary care physicians and driving the to the PCP area of the site. Video clips of the cognitive assessment tool could be effective in driving traffic and attracting new site audiences

- **Activate Partner Networks**
  - Partner with the American Academy of Family Physicians to explore opportunities to post sponsored content on their site driving back to the new resources, guest blog on their website, advertise in their print and digital publications and more
  - Develop social media posts to share with MBIs and other partners, encouraging them to post and share with their networks
  - Develop web banners MBIs and other partners can post to their websites linking to the PCP are of the MBRF website

Education Statement

April 9, 2020

The McKnight Brain Research Foundation is the only private foundation dedicated exclusively to discovering the mysteries of the aging brain and helping people achieve a lifetime of cognitive health[1]. Elevating public awareness and understanding of cognitive aging and age-related memory loss is one of the Foundation's highest priorities. To meet this mission, we're working to fill the educational gaps and help primary care physicians recognize the signs of cognitive aging and age-related cognitive decline in order to help patients take action to maintain their brain health[1a/3a].

While one in eight people age 65 and older (13 percent) develops Alzheimer's disease, the remaining 87 percent are experiencing cognitive changes attributable to the normal aging process to varying degrees[2]. Unlike Alzheimer's disease and other neurodegenerative diseases, cognitive aging is not defined by a neurological or psychiatric disease or process[2a]. The brain changes associated with aging are part of a natural process that starts at birth and continues throughout the lifespan[2b]. While the brain ages just like the rest of the body, there is increasing evidence that cognition and brain health can be maintained with behavioral and lifestyle changes.

As the first point of contact to interact with patients, primary care physicians are best positioned to identify patients at-risk for or experiencing cognitive changes due to aging[3]. With the information and resources provided by the MBRF, they can and should be able to recommend or conduct screening during wellness visits and offer diet, exercise and lifestyle changes that have been proven to help maintain brain health[4/4a]. To learn more about these evidence-based recommendations and the importance of screening for cognitive changes, please visit the McKnight Brain Research Foundation website at: mcknightbrain.org[5/5a].

1. Intro to MBRF and our interest and role
    a. State our plan/intent to increase awareness and work to fill education needs/gaps for primary care
2. Note the large percentage that have CA/ML vs pathologies
    a. Note the difference between cognitive aging/memory loss and pathologies like Alzheimer's disease 87/13
    b. Define age-related memory loss
3. Note role that primary care has in being "front line" seeing these patients
    a. Note the need to increase awareness and education of primary care in this area
4. Cite the benefits and importance of screening during wellness visits by primary care
    a. Reinforce evidence-based recommendations like sleep, diet, activity etc
5. Link to the website resources, tools exist for assessment
    a. Recommend well validated tools for primary care

Content Outline for Primary Care Physicians Area of the McKnight Brain Website
June 4, 2020

Overview

The McKnight Brain Research Foundation seeks to develop a designated area of its website with tools and resources to help fill educational gaps and assist primary care physicians in identifying patients at-risk for or experiencing cognitive changes due to aging. Using the information and resources provided on the website, primary care physicians will also be able to recommend or conduct cognitive screening during wellness visits and offer tips on the diet, exercise and lifestyle changes that have been proven to help maintain brain health.

Suggested Content and Resources

What is Cognitive Aging?

- Cognitive Aging 101
- General Facts on Aging/Brain Health
- Benefits of Maintaining Brain Health
- Warning Signs and Behavior Changes

Prevention

- How to Maintain Brain Health
- Exercise for Brain Health
- Brain Healthy Diet Tips

Research Snapshots

- Highlight research from McKnight Trustees or MBI scientists with patient implications

Cognitive Assessment

- Importance of Cognitive Assessment
- Warning Signs
- Online Assessment Tool (3 options)
    - Link to outside trusted resources with descriptions of what each tool does and the differences
    - Create an online form – series of 10 questions PCPs can ask patients and a scoring tool based on the questions results
    - Create our own online assessment tool – PCPs and patients can walk through the McKnight Brain Assessment Tool together and question results will generate a doctor/patient recommendation upon completion

Patient Resources

- Fact Sheets and Resources to pass along to patients showing signs of cognitive decline and age-related memory loss:
    - How to Talk to Your Doctor
    - Treatment Options
    - Lifestyle Tips to Maintain Brain Health

KEY MESSAGES FOR PRIMARY CARE PROVIDERS (PCPs)
MARCH 2023

Below are a set of recommended action steps primary care providers can proactively take during annual wellness visits or otherwise with adult patients of all ages to protect their patients' brain health.

Cognitive aging happens over a lifetime, and therefore patients should be encouraged at all ages, even as early as their 20s, 30s, and 40s, to pay attention to and mitigate risk factors to help them maintain brain health. The main source for the recommendations below is *Cognitive Aging – Progress in Understand and Opportunities for Action* (2015), a publication of the Institute of Medicine of the National Academies (found here).

1. Steps that Primary Care Providers can take to Promote Brain Health

- Use the Annual Wellness Visit as an opportunity to conduct preventive screenings including cognitive assessments. An overview of some of the more widely-used cognitive assessments can be found on the MBRF website. For additional information on how to code and bill for these assessments, visit Gerontological Society of America's KAER Toolkit, pgs. 3-8
- Educate patients about **health-promoting behaviors** which may reduce the risks of cognitive decline. Research-based recommendations include:
    - Staying physically active;
    - Reducing and managing cardiovascular disease risk factors including tight blood pressure control, weight reduction, cessation of smoking, and lowering cholesterol levels;
    - Encouraging family members to report any noticeable changes in the patient's cognitive abilities or memory;
    - Regularly reviewing any pertinent health conditions, medications, or supplements which may impact the patient's cognitive health;
    - Encouraging the patient to stay socially and intellectually engaged;
    - Discussing stress management and encouraging the patient to seek medical attention for any symptoms of depression, anxiety or any other mental health concerns;
    - Encourage eating a healthy and balanced diet that's low in fat and high in vegetables and fruit; and
    - Encourage getting the recommended amount of sleep while ruling out possible sleep disorders.

- Educate patients about **risk factors** which may increase the risk of cognitive decline. Research-based recommendations include:

    - Talk with patients about unhealthy behaviors that increase the risk of cognitive decline, such as cigarette smoking, excessive alcohol consumption, and a sedentary lifestyle;
    - Share evidence-based information regarding products that may be harmful or without benefit, including nutraceuticals and other interventions (PCPs may consult this evidenced-based web site on "Complementary Remedies" for older adults and Table 1 of this American Family Physician Article).

- Talk with your patients about the medicines they take and discuss possible side effects they may have on their memory, sleep and brain function (a helpful resource for this conversation is the Administration for Community Living's publication, "Brain Health: Medicine, Age, and Your Brain");

- Address perceptions, fears and common misunderstandings about aging and cognitive decline (for helpful tips on having this conversation, see Gerontological Society of America's KAER Toolkit, pages 11-12 and the National Institute on Aging's "Talking with your Older Patients");
- Intervene to minimize cognitive decline associated with medical conditions such as stroke, diabetes, head trauma, renal insufficiency, vision and hearing losses and cardiac disease;
- Upon admission to the hospital, screen for delirium risk factors and implement delirium-prevention strategies.

2. PCP Resources and Patient Handouts

Below are helpful handouts and resources that can be shared digitally, or in print, with patients:

- The MBRF's brochures explain the concepts of brain health and cognitive aging and include healthy lifestyle recommendations that benefit brain health.
  - "Keeping Your Brain Healthy" (digital and print, brochure)
  - "Cognitive Aging Explained" (digital and print, brochure, *in development*)
  - "Top 10 Tips for Healthy Aging" (digital and print, tips sheet)
- National Institute on Aging (NIA)
  - Cognitive Health and Older Adults (article)
  - What Do We Know about Healthy Aging? (article)
  - A variety of "Free Publications" produced by the NIA can be found here
- U.S. Department of Health and Human Services, Administration for Community Living (ACL)'s handouts review the basics of brain health:
  - "Talking About Brain Health And Aging - The Basics" (handout)
  - "Talking About Brain Health And Aging - The Basics" (PowerPoint Presentation for Providers and Educators)
  - "Brain Health: Medicine, Age, and Your Brain" (handout)
- American Heart Association's "Life's Essential 8™ Fact Sheet" (handout)

3. The Case for educating patients about their Brain Health

Overwhelmingly, Americans report wanting to learn how to "stay sharp," yet also report having little awareness about brain health research. PCPs can be the accessible, trusted, and familiar conduit of information and guidance on lifestyle habits and changes that patients can make to maintain and preserve their brain health.

Two-thirds of individuals report having little or no knowledge about brain health research (August 2022)

Commissioned by Research!America in partnership with the Dana Foundation, an August 2022 national survey captured Americans views on brain health and brain health research. Despite the widespread personal impact of brain health issues, 66% of respondents reported having little or no knowledge about brain health research. Of interest is that the same percentage of respondents, 66%, indicated strong curiosity to learn more. (Source)

"The 87%", The Journals of Gerontology, Series A, Vol 67, Issue 7, July 2012 - Molly V. Wagster, PhD, et al

- One in eight people 65 and older (13 percent) develops Alzheimer's disease.
- The remaining 87 percent are experiencing cognitive changes attributable to the normal aging process to varying degrees.

AARP 2016 Member Opinion Survey Results

- 84 percent of members surveyed (age 50 and older) were very concerned with staying mentally sharp.
- Staying mentally sharp (90 percent) and physically fit (87 percent) were the top two health/self-related interests among those surveyed.

KEY MESSAGES FOR CONSUMERS
MARCH 2023

The information below can be shared with individuals, family members, and caregivers to help advance their knowledge around cognitive aging and the steps they can take to preserve their brain health. Even small lifestyle changes can have significant benefits and may help older adults maintain their cognitive health. Research shows that a combination of these healthy behaviors may also reduce the risk of developing dementia. (Source)

Cognitive Aging Scientific Summary Statements

- Cognitive aging refers to the effect age has on cognition – including memory, thinking, learning, and problem solving – and is a normal part of getting older
- Cognitive aging affects individuals differently. Whereas some individuals experience cognitive changes in memory, for example, other may experience changes in other domains (e.g., proc speed, attention)
- The effects of cognitive aging may impact a person in subtle ways, such as not instantly finding the right word, or forgetting where you put your glasses.
- Cognitive training and physical activity interventions show promise for delaying or slowing age-related cognitive decline. (*Cognitive training is defined as a broad set of interventions, such as those aimed at enhancing reasoning, memory, and speed of processing.*)[1]
- The science of cognitive aging is still developing.

Key Messages for Consumers

1. What is Cognitive Aging?
As we age, our brains age too. Cognitive aging, like aging in general, is a natural process.

- Our brains age at different rates and in different ways.
  - Wisdom, expertise and vocabulary typically increase with age, while other abilities like processing speed, decision-making and some types of memory may decline.
  - The brain changes associated with aging are part of a natural process that takes place throughout our lives.
- Cognitive health is the ability to clearly think, solve problems, learn and remember. It's just one aspect of overall brain health and is an important part of protecting your ability to perform everyday tasks.

2. What is Brain Health?
Brain health is how well your brain functions across several areas, including:

- How well you think, learn and remember;
- How well you control your body movement, including balance;
- How well you interpret and respond to emotions; and

[1] National Academies of Sciences, E., et al., in *Preventing Cognitive Decline and Dementia: A Way Forward*, A. Downey, et al., Editors. 2017, National Academies Press (US)

- How well you make effective decisions.

3. What Can You Do to Maintain Brain Health?

- It's never too soon or too late to protect your brain health. Taking steps now, like staying physically active, getting enough sleep, and reducing and managing your risk for cardiovascular disease can help maintain your brain health as you age.

- Growing evidence shows there are various lifestyle behaviors that may help protect your brain health now and in the future. (Sources include National Institute on Aging and American Heart Association):
    1. **Exercise --** Break a sweat and engage in regular cardiovascular exercise that elevates the heart rate and increases blood flow to the brain and body.
    2. **Quitting Smoking –** Reduce your risk of cognitive decline to levels comparable with those who never smoked.
    3. **Keeping a Healthy Heart --** The risk factors for cardiovascular disease and stroke — obesity, high blood pressure, and diabetes — also have been shown to negatively impact cognitive health. Preventing and managing high blood pressure and cholesterol will help protect the heart and take care of the brain.
    4. **Eating a Healthy and Balanced Diet –** Following a diet that's low in fat and high in vegetables and fruit has also been linked to reducing the risk of cognitive decline. Although research on diet and cognitive function is limited, certain diets, like the Mediterranean and Mediterranean-DASH (Dietary Approaches to Stop Hypertension), may help maintain brain health.
    5. **Getting Enough Sleep –** Not getting enough sleep may result in problems with memory and thinking, yet a third of American adults report regularly getting less than the recommended 7-8 hours of sleep. Help protect your brain by getting better sleep.
    6. **Staying Socially Engaged –** Social and intellectual engagement is important for brain health. Pursuing interesting and meaningful social activities will help you keep connections with others. Try volunteering at a local church or animal shelter or just share the activities you enjoy with friends and family.
    7. **Learning and Welcoming Challenges –** Challenging and activating the mind by reading, doing puzzles, building furniture, or playing games are good ways to encourage strategic thinking. Taking an online class or learning a new language will also help keep your mind sharp.
    8. **Don't Forget Mental Health** -- Some studies also link depression with increased risk of cognitive decline. Managing stress and seeking medical attention for any symptoms of depression, anxiety or any other mental health concerns will help optimize your brain health.

3. Consumers' Concern with Cognitive Aging and Memory Loss/Prevalence and Desire to Learn More

Given the lack of data quantifying the number of people affected by cognitive aging and the associated cost, the statistics below can be used to help frame the issue in terms of prevalence and concern.

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- Despite the widespread personal impact of brain health issues, 66% of respondents reported having little or no knowledge about brain health research. Of interest is that the same percentage of respondents, 66%, indicated strong curiosity to learn more. (Source)

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McKnight Brain Research Foundation Mid-Career Research Award in Cognitive Aging and Memory Loss

Founded in 1999 by Evelyn F. McKnight, the specific goal of the McKnight Brain Research Foundation (MBRF) is to better understand and alleviate age-related cognitive decline and memory loss.

While it has been stated that one in eight people 65 and older has Alzheimer's Disease, cognitive changes due to the normal aging process will affect many of the remaining 87%, impacting abilities like processing speed and decision-making and contributing to some types of memory loss. The McKnight Brain Research Foundation champions research to better understand age-related cognitive decline and memory loss and educate the public on how to maintain cognition and brain health while aging successfully.

As the only private foundation focused exclusively on differentiating cognitive aging, age-related cognitive decline and memory loss from pathological disease states, (such as Alzheimer's disease and related dementias), the MBRF has established a national platform for outreach to the scientific community and the public. To accelerate the mission of the MBRF, the Foundation has previously partnered with other institutions to establish McKnight Brain Institutes at the University of Alabama at Birmingham, the University of Arizona, the University of Miami, and the University of Florida.

The McKnight Brain Research Foundation and the McKnight Brain Institutes are leaders in cognitive aging research. Together, they are committed to sharing innovations in research and practical suggestions for maintaining brain health with the public, while supporting research leading to better understanding and alleviating age-related cognitive decline and memory loss.

OUR COMMITMENT TO RESEARCH

With direct contributions from the MBRF and strategic initiatives led by the MBRF through partnerships with the National Institute on Aging through the Foundation for the National Institutes of Health, and the four McKnight Brain Institutes, more than $180 million dollars have been provided in funding research specifically targeted towards cognitive aging, age-related cognitive decline and memory loss. By supporting three Cognitive Aging Summits and commissioning the National Academy of Medicine's study and report on Cognitive Aging (https://www.nap.edu/catalog/21693/cognitive-aging-progress-in-understanding-and-opportunities-for-action), the Foundation has made great progress leading to the understanding and alleviation of the effects of age-related cognitive decline and memory loss over the last two decades.

In fulfilling its mission of *"nurturing scientists dedicated to exploring and pursuing innovative research to advance the understanding and alleviation of age-related memory loss"*, the MBRF has partnered with the American Academy of Neurology through the American Brain Foundation to fund two cognitive aging clinical translational research scholarships per year for five years. The program is designed to support physicians or PhDs who are committed to a research program in cognitive aging and memory loss and have completed their training within five years of application. Each scholarship is a two-year award for a total of $150,000. In addition to the Scholarship program, the MBRF has previously funded individual block grant research support for inter-institutional collaborators between the four McKnight Brain Institutes.

The MBRF now proposes to extend its mission of supporting the next generation of world-class research scientists in the field of cognitive aging and memory loss by targeting outstanding mid-career scientists who have already demonstrated a firm commitment to cognitive aging research. This group of scientists is at a key milestone in their career trajectory having already proven themselves to be committed to research in cognitive aging and clearly demonstrated their potential to become leaders in their field. By providing research funding to these promising investigators as they continue to embark upon independent careers, the MBRF proposes to build a core group of outstanding research scientists across the United States with the potential to lead transformative research in the field of cognitive aging.

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PROPOSAL

The MBRF proposes to establish the ***McKnight Brain Research Foundation Mid-Career Research Award in Cognitive Aging and Memory Loss***

a. Length of Award: three years, renewal annually after satisfactory review

b. Amount of Award: $250,000 per year with match from the host institution

c. The Foundation commits to funding the program for a five-year initial trial period which would have supported 6 scientists at the conclusion of the five-year cycle

BUDGET

Year 1	Two Awards	$500,000
Year 2	Four Awards	$1,000,000
Year 3	Six Awards	$1,500,000
Year 4	Four Awards	$1,000,000
Year 5	Two Awards	$500,000
MBRF Commitment		$4,500,000

ELIGIBILITY

All applicants for the award program must have:

- completed research/clinical training i.e. formal post-doctoral research training post-PhD and/or physicians who have completed post-residency fellowship training.
- a proven track record of research accomplishments in cognitive aging as indicated by their publications in high-impact journals, awards, and other metrics of peer recognition.
- tenure-track faculty in an academic institution in the United States with evidence of long-term institutional support as indicated by commitment of resources including laboratory space, start-up research funds and personnel. Candidates not in a tenure-track position are also eligible and should also demonstrate similar evidence of long-term institutional support and not be in a time-limited appointment.

The proposed MBRF initiative would add substantial start-up support for a period of three years to help these investigators develop and/or expand an outstanding research program in cognitive aging and memory loss. Each year, one award will be made to support studies focusing on clinical translational research and another toward understanding basic biological mechanisms underlying cognitive aging and age-related memory loss. For example, this support could be deployed towards conducting a pilot clinical trial, developing proof-of concept interventions to ameliorate age associated cognitive impairment, gather preclinical data to accelerate testing of potential interventions, and further study the mechanistic basis of age-associated cognitive impairment with a view to identifying novel treatment targets. Scientists proposing to pursue basic research should clearly articulate the potential of their findings to be translated.

For Immediate Release:

Contact: John Chaich
john@afar.org

AFAR and the McKnight Brain Research Foundation launch new grant program in Cognitive Aging and Memory Loss

New program encourages outstanding mid-career scientists to lead transformative research in the field of cognitive aging.

NEW YORK and ORLANDO— The American Federation for Aging Research (AFAR) and the McKnight Brain Research Foundation (MBRF) are pleased to announce the launch of a new grant award program, **The McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss.**

The MBRF Innovator Awards in Cognitive Aging and Memory Loss are supported by a $4.5 million grant from the McKnight Brain Research Foundation and will support six investigators over a period of five years. Each year, MBRF and AFAR will provide up to two three-year awards of $250,000 annually. The total award amount of $750,000 over the three-year period will add substantial start-up support to help mid-career scientists develop and/or expand outstanding research programs in cognitive aging and memory loss.

The awards will be given in three grant cycles, in which each year, one award will be made to support studies focusing on clinical translational research and another award toward understanding basic biological mechanisms underlying cognitive aging and age-related memory loss.

“For most Americans, staying ‘mentally sharp’ as they age is a very high priority,” said Michael Dockery, MD, Chair of the McKnight Brain Research Foundation board of trustees. “Even those not affected by Alzheimer’s disease or other dementias will likely undergo cognitive changes due to the normal aging process. With the population of older adults growing rapidly in the United States and across the globe, it is critical that we support researchers dedicated to better understanding and alleviating the effects of age-related cognitive decline and memory loss.”

AFAR has long supported the careers of talented investigators and research on cognitive health. “By providing research funding, AFAR and MRBF are building a cadre of outstanding research scientists across the United States who have the potential to lead transformative research in the field of cognitive aging,” says Stephanie Lederman, EdM, Executive Director, AFAR.

With the new program, MBRF is extending its mission of supporting the next generation of world-class research scientists in the field of cognitive aging and memory loss by targeting outstanding mid-career scientists who have already demonstrated a firm commitment to cognitive aging research and shown the potential to become leaders in the field.

“Providing funding at the mid-career stage capitalizes on a unique opportunity to encourage leading scientists to continue embarking on independent careers that will lead to faster development of new ideas and approaches in cognitive aging research than is possible with traditional funding,” notes Lederman.

“We are excited to partner with AFAR and look forward to seeing the impact of the research bolstered through the new Innovator Awards in Cognitive Aging and Memory Loss,” Dockery added.

More information on the grant program and application can be found here: www.afar.org/grants/mcknight-award.

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About AFAR
The American Federation for Aging Research (AFAR) is a national non-profit organization that supports and advances pioneering biomedical research that is revolutionizing how we live healthier and longer. For four decades, AFAR has served as the field's talent incubator, providing more than $184 million to more than 4,200 investigators at premier research institutions nationwide. A trusted leader and strategist, AFAR also works with public and private funders to steer high quality grant programs and interdisciplinary research networks. AFAR-funded researchers are finding that modifying basic cellular processes can delay—or even prevent—many chronic diseases, often at the same time. They are discovering that it is never too late—or too early—to improve health. This groundbreaking science is paving the way for innovative new therapies that promise to improve and extend our quality of life—at any age. Learn more at www.afar.org or follow AFARorg on Twitter and Facebook.

About the McKnight Brain Research Foundation
Founded in 1999, the McKnight Brain Research Foundation is the nation's only private foundation devoted exclusively to discovering the mysteries of the aging brain. By supporting research and investigation, we're working to better understand and alleviate the effects of age-related cognitive decline and memory loss. Learn more about the Foundation at: www.mcknightbrain.org.

Meet the 2022 Innovator Award Recipients
https://mcknightbrain.org/innovator-award-recipients/

Emilie Reas, PhD, Professor, University of California, San Diego

Project: *The mediating role of bloodbrain barrier dysfunction in effects of systemic inflammation on brain microstructure and memory*

Dr. Reas' lab uses advanced brain imaging methods to develop biomarkers of early Alzheimer's disease and to characterize the neurobiological changes leading to brain aging and dementia. Although inflammation and vascular dysfunction are risk factors for dementia, it remains unclear how they promote cognitive decline. Given the brain's privileged protection from the periphery by the "blood-brain barrier," the ways by which systemic inflammation affects the brain remains a critical unanswered question.

With support from the 2022 Innovator Award, Dr. Reas will examine relationships of blood-borne inflammatory factors with microstructural brain injury and memory, and to determine if a leaky blood-brain barrier mediates these associations. She will also evaluate whether individuals with high genetic risk for Alzheimer's disease show stronger connections between inflammation and brain microstructure, vascular leakage, and memory impairment.

Findings are expected to clarify how inflammation and vascular dysfunction accelerate brain aging, and to guide development of therapeutic approaches to optimize cognitive health with age.

Tara Tracy, PhD, Assistant Professor, Buck Institute for Research on Aging

Project: *Role of KIBRA in Age-Related Memory Loss*

The dynamic modulation of the synaptic connections between neurons in the brain is critical for memory. Decline in synapse function underlies memory loss in aging, but little is known about what factors make synapses more vulnerable to dysfunction with age. KIBRA (KIdney/BRAin) is a postsynaptic protein required for synaptic plasticity and memory. Genetic variation in KIBRA is associated with age-related memory deficits in older adults. Given the critical role of KIBRA protein at synapses, the amount of KIBRA expressed in the brain may modulate susceptibility to memory decline in aging.

With funding from the 2022 Innovator Award, Dr. Tracy's lab will investigate how KIBRA levels impact synapse dysfunction and memory loss in aging. The goal of this research is to uncover mechanistic insight into the susceptibility of synapses to dysregulation in aging which could guide development of a therapeutic approach to repair synapse function as a treatment for age-related memory loss.

To learn more about the Innovator Awards or to apply please go to:

https://mcknightbrain.org/innovator-awards-in-cognitive-aging/

https://www.afar.org/grants/mcknight-award.

Communications Outreach Program

McKNIGHT BRAIN RESEARCH FOUNDATION

Preserving memory, enhancing life

TWO YEAR COMMUNICATIONS PLAN

July 2021 – July 2023

Approved October 28, 2021

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OVERVIEW

- The McKnight Brain Research Foundation is a leader in the field of age-related cognitive decline and memory loss and the only foundation dedicated exclusively to solving the mysteries of the aging brain and helping people achieve a lifetime of cognitive health
- With elevating public awareness and understanding of cognitive aging and age-related memory loss as one of the Foundation's highest priorities, the timing is right to build on the communications initiatives started in 2019 with another two-year communications plan
- Assets developed and experience gained over the past two years provide the platform to establish a national presence and elevate the McKnight Brain Research Foundation to become a household name

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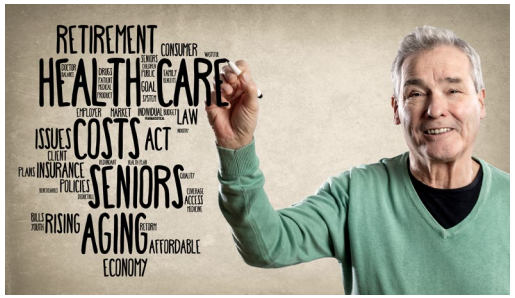
OPPORTUNITY

Over the past two years, the McKnight Brain Research Foundation has developed content and programs targeting consumers, primary care physicians and researchers:

- Launched a new **consumer friendly** brand identity and website with educational and engaging content
- Added a dedicated section of the website targeting **primary care physicians** as the ideal audience to recognize the signs of cognitive aging and memory loss and help patients take action to protect their brain health
- Started the MBRF Innovator Awards in Cognitive Aging and Memory Loss program, enhancing its current scholarship offerings and **reinforcing its commitment to researchers** across the career-span working to better understand and alleviate age-related cognitive decline and memory loss



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RECOMMENDED APPROACH

Leveraging the McKnight Brain Research Foundation's newly developed assets and the public's continued interest in aging successfully, the timing is right to commit to a new **two-year communications program**

The Approach – Implement a visibility program to generate national awareness for the Foundation's commitment to alleviating the effects of age-related cognitive decline and memory loss by:

- **Educating the public** on cognitive aging and how to maintain brain health
- **Raising awareness among primary care physicians** for the importance of identifying patients at-risk of or experiencing cognitive changes due to aging
- **Highlighting researchers** committed to advances in better understanding and preventing cognitive decline and age-related memory loss

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COMMUNICATIONS OBJECTIVES

- Continue working to build and establish the McKnight Brain Research Foundation name among primary care physicians, as well as with older adults, caregivers and the general public
- Establish a clear brand identity, presence and messaging strategy
- Grow and foster consumer awareness on cognitive aging through social media and marketing efforts positioning the McKnight Brain Research Foundation as the key resource on the topic
- Continue developing fresh online content to educate the public on the importance of brain health and how to reduce the effects of cognitive aging
- Leverage timely news and announcements related to brain health to establish a voice for the Foundation as a thought leader

CAMPAIGN AT-A-GLANCE

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YEAR ONE: LEVERAGE & REFINE EXISTING ASSETS

- Develop a patient-friendly brochure as a comprehensive guide to maintaining brain health and preventing the effects of cognitive aging
- Launch a consistent social media promotion campaign through the month of September timed to Healthy Aging Month
- Survey primary care physicians on their needs and use feedback to refine dedicated section of website
- Work with the MBIs to identify a network of expert researchers tied to specific content areas to interview for the Ask the Experts blog series and offer as media spokespeople
- Promote new and existing programs and leverage research announcements on the horizon to generate visibility opportunities and build the organization's position with media
- Track and evaluate reach and outreach success as a baseline to set growth and engagement goals for 2022

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YEAR TWO: CONTINUOUS CROSS CHANNEL PROMOTION

- Consistent year-round media outreach offering MBRF and MBI experts to comment on emerging research and key moments in time
- Continued online and social content development to engage and educate consumers on brain health and ways to stay sharp
- Primary care physician outreach, education and engagement
- Ongoing measurement to track success and build growth strategy

YEAR ONE ACTIVITIES

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REACH & ENGAGE CONSUMERS

Develop and promote new materials targeting consumers

- Develop a patient-friendly brochure as a leading resource on optimizing brain health and preventing cognitive decline
- Develop monthly content themes and use to draft consumer-friendly blog posts, social media content and new web pages
- Continue building list of interested consumers and launch quarterly newsletter in Q1 of 2022

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DRIVE TRAFFIC TO ONLINE RESOUR

Launch a dedicated month-long social media outreach campaign in September tied to *Healthy Aging Month*

Key Learnings

The two-week campaign promoting Dr. Sanjay Gupta's video interview increased daily site traffic by ***600 percent***

Lessons from that campaign were applied to develop a ***month-long social media outreach campaign in September*** driving traffic to McKnightBrain.org and adding followers to the Foundation's social media channels

June is already crowded with Alzheimer's messages

September offers an opportunity for the Foundation to ***take ownership and become a primary resource*** for a key awareness month

Grassroots approach in September of 2021 leveraged remaining Sanjay Gupta campaign funds and reached nearly 7,000 people via Facebook and generated more than 2,000 post engagements

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EDUCATE THE MEDICAL COMMUNITY

The McKnight Brain Research Foundation has developed content specifically to get *primary care physicians* thinking more about age-related cognitive decline and memory loss and needs to take steps to *engage the medical community*

- Survey primary care physicians to better understand their needs when it comes to brain health
- Refine and update the primary care section of the website to reflect key learnings
- Identify leading experts to interview for blog posts and videos to drive traffic to the site

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COMMITMENT TO RESEARCH

Highlight the *McKnight Brain Research Foundation's 20+ year commitment to research* by:

- Launching and promoting the new ***Innovator Awards program*** and profiling scholarship recipients as selected
- Continue promoting the ***McKnight Clinical Translational Research Scholarship program*** and touting scholarship awardees
- Leveraging ***announcements of emerging research in the field*** when media will already be focused on the topic to establish a clear voice for MBRF
- Positioning ***Foundation spokespeople as thought leaders*** by commenting on announcements and offering perspective on their significance

YEAR TWO SNAPSHOT

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YEAR TWO SNAPSHOT

Continuous Cross Channel Promotion

Continue ***building brand recognition*** for the McKnight Brain Research Foundation with the goal of establishing the organization as **the** primary resource on cognitive aging

- Identify monthly themes and build supporting content to ***drive consumer engagement*** via the website and social media channels
- Continue ***social media outreach*** to complement outreach calendar initiatives and consistently share MBRF news, updates and educational content
- Launch a quarterly webinar or video interview series to ***educate and engage primary care physicians*** and drive them to McKnightBrain.org for resources and pass-along information for patients
- Continue ***highlighting the Foundation's commitment to research*** through thought leadership initiatives and scholarship promotions

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THANK YOU!

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Communications Plan Budget Breakdown
Year Two July 2022 – July 2023

Activities	Total Budget: $270,000
Dedicated communications professional	√
Web support and site maintenance	√
Creative development for patient brochure	√
Limited strategy and graphic design for grassroots social media campaigns	√
Video development and support	√
AAN advertising to announce the McKnight CTRS application period	√
Researching industry trends and events to inform content strategy	√
Creating a calendar of suggested content to be shared across MBRF's social channels (calendar to include post topics, title, blurb and related links for MBRF to build out and make posts)	√
Developing creative assets for monthly social media posts	√ **1-2/week**
Developing creative assets for consumer blog posts	√ **quarterly**
Designing newsletter template and providing backend implementation support	√
Developing creative assets, content strategy and support for the consumer newsletter	√ **quarterly**
Tying content strategy, social content and blog strategy together to execute paid social media campaigns	√ **two/year**
Advising the ad spend strategy for paid social media campaigns	√ **two/year**
Hosting and managing primary care webinar/video interview series	

Ask the Experts Blog Series

https://mcknightbrain.org/blog/

Overview:

The Ask the Experts blog series was added to the McKnight Brain website in 2022 to feature the doctors and scientists behind the effort to better understand and alleviate age-related cognitive decline and memory loss. The blog posts are based on interviews with experts from the McKnight Brain Institutes and examine key issues around cognition and brain health from diverse perspectives.

Experts Currently Featured:

Dr. Steven DeKosky, University of Florida

Dr. Carol Barnes, University of Arizona

Dr. Ronald Lazar, University of Alabama at Birmingham

Dr. Michael Saag, University of Alabama at Birmingham

Upcoming Posts:

Dr. Tatjana Rundek, University of Miami

Dr. Ronald Lazar, University of Alabama at Birmingham, Brain Health Advocacy Mission

Dr. Jennifer Bizon, University of Florida

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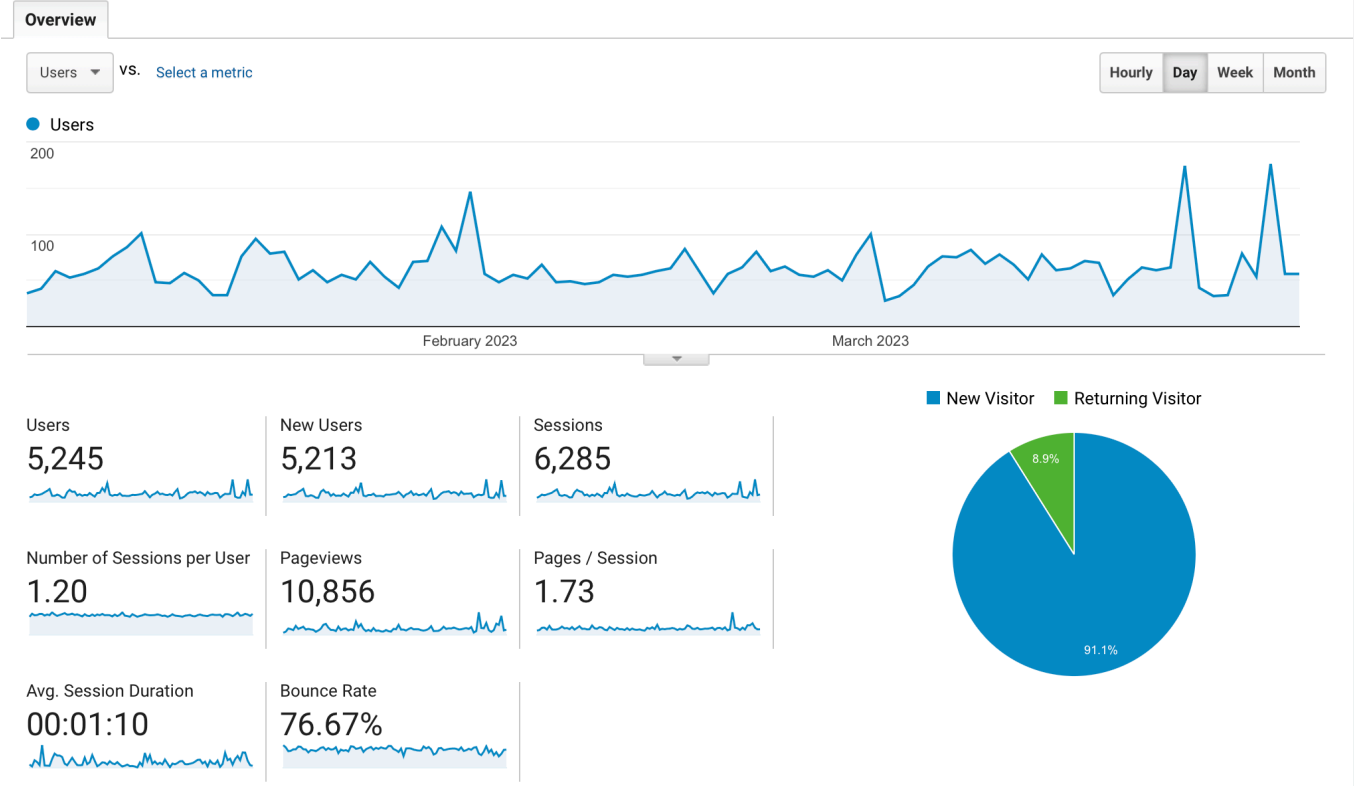
2023 McKnightBrain.org Traffic Report

	January	February	March	Q1 Totals
Users	1,792	1,613	1,906	5,245
Sessions	2,156	1,856	2,273	6,285
Page Views	3,700	2,882	4,274	10,856
Session Duration	1:16	:54	1:17	1:10

Q1 2023 McKnightBrain.org Traffic Totals



Definition of Key Terms

User: Any person who has visited the website. The moment a person lands on any page of the site, they are identified as a User.

Page Views: Total number of pages loaded by Users on the website, including when Users load the same page of the website.

Sessions: A group of user interactions within the website that take place within a given time frame. A single session may include multiple page views, events and social interactions. Sessions track the number of times a user interacts with the website.

Session Duration: How long a visitor remains on the website. Average session duration for direct traffic is 44 seconds.

2023 Media Highlights

Lindsay De Biase honored by McKnight Brain Research Foundation, UCLA Newsroom, April 4, 2023: https://newsroom.ucla.edu/dept/faculty/de-biase-2021-mcknight-brain-research-foundation-award

Giving for Neuroscience Research, Inside Philanthropy, March 15: https://www.insidephilanthropy.com/state-of-american-philanthropy-pdfs/giving-for-neuroscience-research

What We Learned from a Deep Dive Into Neuroscience Research, Inside Philanthropy, March 7: https://www.insidephilanthropy.com/state-of-american-philanthropy-pdfs/giving-for-neuroscience-research

Three Year Communications Plan Proposal and Budget
2023 - 2026

Executive Summary

With approval from the Communications Committee, a Request for Proposal for a Three-Year Communications Initiative was fielded to five communications agencies – BRG Communications, JPA Health, Qorvis, SCP and Whereoware. All five agencies expressed interest and excitement around the project and submitted proposals in time to meet the RFP deadline.

After reviewing the five proposals, two of the proposals submitted did not demonstrate the same level of creative thinking and background understanding of the MBRF and the field of cognitive aging. The proposals from Qorvis and Whereoware addressed the tactical components requested in the RFP, but didn't demonstrate how the agencies would work in partnership with the MBRF to better understand the issue area, craft unique messages, and successfully implement a measurable three-year campaign. For those reasons, the proposals from Qorvis and Whereoware were not presented to the Communications Committee for review.

Based on the submitted proposals and introductory conversations, BRG, JPA and SCP all appeared to be strong potential partners for the MBRF communications initiative. They all presented very structured, detailed and well-thought-out proposals that demonstrated a strong understanding of the goals of the initiative, clearly outlined strategies and tactics to achieve our goals, innovative ideas, and strong background experience conducting large-scale communications initiatives. They all have decades of experience with high-profile national clients and focus on the health, wellness and aging space. Pages 2-5, below, offer a brief summary of the three proposals, and the chart that follows compares the responses using a numeric grade to show the relative strengths of each agency across specific categories. The charts on pages 6-8 outline the projected measurable outcomes each agency anticipates being able to achieve across the three different budget levels.

The Communications Committee reviewed this memo and the proposal materials as reference. At its meeting on April 19, 2023, the Committee discussed the process that was followed to review and evaluate the proposals – including the rankings and comparisons below, in addition to interviews with each of the three agencies conducted by Angelika Schlanger and Valerie Patmintra.

Based on the information presented by Angelika Schlanger and Valerie Patminta, the Communications Committee agreed that while SCP has a very impressive list of clients in the aging and brain health space and clearly demonstrated an ability to secure and implement strategic partnerships that would advance the MBRF's goals of brand and issue awareness, they didn't demonstrate the same level of strength and expertise in conducting multi-year brand awareness campaigns as BRG and JPA. BRG and JPA both demonstrated creative approaches and were excited by the potential of helping the MBRF build its brand reputation and awareness for the importance of brain health, but it was decided that BRG's thorough approach to planning, effective use of budget and confidence in securing high level results gave them a slight advantage over JPA.

The Committee members also discussed the three different budget levels and agreed the mid-tier budget of $1.755 million over three years would be the best starting point to generate a significant increase in outreach and visibility without committing to the highest budget level.

Following this discussion, the committee approved a recommendation to the board to move forward with BRG as MBRF's agency partner at the $1.755M level over three years. This recommendation was submitted to the full Board of Trustees and approved by vote during the Board meeting on May 3, 2023.

BRG Communications Proposal Review

BRG's proposal addressed all requirements of the RFP and highlighted the MBRF's unique positioning to continue advancing research on brain health and cognitive aging, while also raising awareness for the importance of the topic among consumers and primary care providers. BRG conducted a media audit to inform its proposal and found that brain health isn't a clear priority for most competing organizations in the space. By working to differentiate the MBRF messaging from what's currently offered by other organizations, BRG identified the unique opportunity for MBRF to drive behavior change while also building brand visibility.

With clients ranging from Fortune 500 companies to nonprofits, medical societies and industry associations, BRG focuses on communications initiatives to improve how people live through health and wellness. BRG expressed confidence that their team of experts as well as their background and expertise in health behavior change initiatives, make them a strong partner to advance the MBRF's communications efforts.

BRG is an integrated communications agency with in-house experts providing client services, including strategic planning, research and testing, brand strategy, influencer engagement, media relations, social media, digital marketing, content creation, and graphic design. BRG's unique approach to media storytelling consistently results in media impressions and placements that exceed client expectations.

Beyond the objectives we outlined in the RFP, BRG sees the potential to also build strategic partnerships, deepen our engagement with the research community, create a strong network of spokespeople and build relationships with media.

BRG recommends a strong foundation building process including an organizational assessment, marketplace review, program and message architecture development and consensus building to ensure the resulting integrated education and communications program is successful. The assessment findings would be delivered as two facilitated working group sessions to work through program goals and opportunities and used to develop an action plan to drive the communications initiative moving forward.

BRG did not share a suggested theme for the campaign, but said they will develop and share 2-3 creative themes for consideration after the foundation building process is complete. The proposal maps out how BRG would build visibility for MBRF through a range of activities including media relations, thought leadership, healthcare provider and researcher engagement, social media and influencer relationships and strategic partnerships. The proposal clearly describes the opportunity MBRF has to become a leading expert in the brain health field and demonstrates BRG's confidence that they can be a good partner to help us develop and build a successful outreach platform over the long term.

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INITIAL GOALS

CONSENSUS
Align around short-term and long-term activations

AWARENESS
Position MBRF as a leading voice on brain health & cognitive aging

ENGAGEMENT
Leverage key channels & partners to extend reach

IMPACT
Define success and monitor outcomes

YOUR BRAIN HEALTH PROGRAM

Based on our knowledge to date we would build a program that...

- Meets your organization **where you are**
- **Differentiates** from existing initiatives
- Leverages **multiple experts**
- Introduces MBRF brand to **consumers**
- Engages the **healthcare community**
- Relies on a clear **measurement plan**

KEY PROGRAM ELEMENTS

RESEARCH APPROACH
BRG takes an analytical approach to creating and leveraging existing research insights. We do a thorough analysis of the landscape first to see where there may be gaps and opportunities to provide meaningful content. **We build evidence-based programs**, not the other way around.

ROBUST PARTNERSHIP STRATEGY
We take a 360 view of **partnerships that can best advance your goals**. This will include consideration of how to best collaborate with other experts and participate in other initiatives that may advance the cause. We would also build custom recommendations around **media partnerships, partnerships with like-minded organizations and influencer opportunities** that would bring MBRF to market in new ways.

AWARD WINNING MEDIA & SOCIAL
Effective campaigns rely on leveraging a strategic integrated mix of paid, owned, earned and shared content. A **robust news engine** would fuel a wide range of media opportunities targeting a strategic mix of consumer, healthcare, national and trade media. Combine this with our **smart social strategies** and evidence-based content applied across targeted channels, MBRF will have a successful program.

HCP 360
We have deep experience engaging healthcare providers in various specialties. We would reach patients where they are by engaging various specialists and finding unique opportunities to promote messages that **do not always rely on primary care physicians**. We leverage creative opportunities to engage inside and outside the physicians offices – **wherever health conversations are happening.**

WHAT SUCCESS CAN LOOK LIKE

Content & Insights	Web & Social	Strategic Partnership	PR Support	Thought Leadership	HCP Focus	Paid Media
•MBRF owned data •Improved story quality •Consumer awareness •A way to measure impact	•Enhanced web site •Increased web traffic •Quality social engagement •New tools	•Increased credibility •Brand visibility in new channels •Increased web/social activity	•Increased credibility •More visibility for MBRF •Media relationships	•Increased brand reputation •Trained spokespeople •Industry recognition	•Deeper HCP relationships •Increased brand reputation •New partners	•Reach new audiences where they are •Message amplification

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BRG

AS YOUR PARTNER, WE WILL:

- Staff your team with seasoned, tenured experts
- Ask the tough questions to create true success measures
- Leverage existing assets before building new ones
- Maximize your capacity through smart collaborations
- Guarantee no surprise billing
- Deliver quality work and results

250 Industry Awards for Successful Client Campaigns

100% Staff Retention 18+ months

Great Place To Work. Certified FEB 2023-FEB 2024 USA

50% Clients with 5+ year relationship

WHY BRG

- This is the work we are passionate about – our entire business is built around **Communications for Better Living®**
- Our expertise areas are **driving change through awareness & education; promoting data and science; and building brands**
- We have had no staff turn-over for more than a year and half; meaning your team will be able to **go deep, be consistent and reliable**
- We build client relationships that last because **we make our client the hero**, add strategic value, deliver results and make the process painless
- We are the right size agency. MBRF would be an **important client to our leadership and our entire team**

HEALTHCARE EXPERIENCE HIGHLIGHTS

BRG has deep experience developing award winning public health campaigns and promoting scientific data

ACPM American College of Preventive Medicine · aga American Gastroenterological Association · American Diabetes Association. · National Sleep Foundation · ACI · March of Dimes · SCAI · Medtronic · Heart Rhythm Society · CVSHealth · aetna

McKnight Brain Research Foundation (MBRF)

Charter of the Communications Working Group

An Advisory Group to the Board of Trustees

Purpose

The purpose of the Communications Working Group is to advise the McKnight Brain Research Foundation Board of Trustees on strategies to raise the level of public awareness about the importance and value to society of research in cognitive aging and age-related memory loss; to enhance public understanding of maintaining cognitive function and preserving memory; foster greater recognition of the history, achievements and current work of the McKnight Brain Research Foundation (MBRF); highlight the scientific research conducted within the network of McKnight Brain Institutes (MBIs); and share this information with the public in a relatable, engaging manner utilizing the McKnight network of experts.

The Communications Working Group will share expertise and ideas for elevating the McKnight Brain Research Foundation brand, will identify communication tools, resources, and audience segments, develop key messages, identify experts as possible spokespeople, identify media contacts, will suggest research of interest to the public, and will advise and recommend development of materials to share with MBRF and across the MBI network. The Communications Working Group will advise the MBRF Board of Trustees on the feasibility for national outreach including a public awareness campaign and will provide input into a communications plan to be reviewed and approved by the Board of Trustees.

Members

The Communications Working Group shall consist of 1 to 3 members from each McKnight Brain Institute. MBI Leadership shall nominate members who have expertise in one or more of these areas: communications, publications, marketing, website development, digital strategies, public relations, media relations, and/or other externally focused areas. Trustee Members will be appointed by the Chairman of the MBRF and, with the Chairman of the MBRF, these trustees will serve as ex officio members of the Communications Working Group. The Executive Director of the MBRF will serve as Chairman of the Communications Working Group.

Meetings

The Communications Working Group shall meet by phone at those times and places as determined by the membership of the group. The Communications Working Group may meet in person annually at the inter-institutional meeting of the McKnight Brain Institutes as determined by the Trustees of the McKnight Brain Research Foundation.

McKnight Brain Research Foundation and the McKnight Brain Institutes
Communications Working Group Members

May 2023

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Angelika Schlanger
Executive Director
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McKnight Brain Research Foundation Senior Communications Advisor

Duties and Responsibilities

1. MBRF Communications Tools and Materials

- Maintain the MBRF logo and branding across all materials
- Develop new materials as needed, including brochures, fact sheets, FAQs, etc.
- Draft press releases and news announcements

2. MBRF Website and Social Media

- Draft and post new content to maintain the MBRF website
- Interview experts and draft posts for the monthly Ask the Experts blog series
- Develop themes and draft content on a monthly basis to make 3-4 social media posts each week.
- Plan and implement quarterly social media outreach campaigns

3. MBRF Media Outreach and Tracking

- Work with the MBIs to identify research stories and experts for potential media outreach
- Track media and social media metrics and reach throughout the year and provide quarterly updates to the Trustees

4. Communications Working Group

- Schedule and staff bi-monthly meetings with members of the Communications Working Group to engage in ongoing activities, including:
    - Sharing news announcements and research activities
    - Reviewing, vetting and approving MBI communications materials
    - Providing input on upcoming studies with relevant consumer/medical angles
    - Identifying young researchers and studies of note to highlight on the MBRF website and social media channels

Valerie Patmintra
Senior Advisor of Communications
McKnight Brain Research Foundation (MBRF)

Valerie Patmintra is a communications executive with more than 20 years experience developing and implementing successful marketing and communications programs for nonprofit organizations and Fortune 500 companies. Valerie serves as the Senior Advisor of Communications, to the MBRF. In this role, she provides ongoing communications support, including message development and implementation, content development and maintenance of mcknightbrain.org and organizational materials. She also provides social media strategy and content development, and media relations support.

Before beginning her work with the MBRF, Valerie served as the Director of Communications for the National Osteoporosis Foundation. In this position, Valerie developed and implemented the organization's annual marketing communications strategy to build and strengthen its role and reputation as the leading voice on osteoporosis. By building and maintaining national media relationships and serving as the organization's principal point of contact for media, she secured more than 400 million media impressions for the organization on average annually. She also implemented the organization's *Generations of Strength* awareness campaign and managed the public relations agency of record to secure more than 100 million media impressions for three-month campaign.

Valerie also served as the communications director for NOF's partner agency, the National Bone Health Alliance, and implemented the organization's first national awareness campaign, which resulted in more than 200 million media impressions with placements in top tier media outlets, including *Wall Street Journal*, *Associated Press* and *USA Today*.

Prior to joining NOF, Valerie served as a Senior Account Director for BRG Communications and led teams to develop award-winning national awareness campaigns for corporate and nonprofit clients, including the Home Safety Council, National Center for Healthy Housing, Medtronic and the American Osteopathic Association. She managed proactive and reactive media relations, resulting in feature segments and stories with top-tier media outlets, including The Today Show, *Good Housekeeping,* and *USA Today.* Valerie also developed and implemented the public relations and organizational communications strategy for the Home Safety Council's Silver Anvil award-winning Home Safety Month campaign that resulted in 200 million media impressions on average annually.

Valerie also served as a senior consultant with Booz Allen Hamilton and worked on teams supporting Kodak, SAP, and the Consumer Electronics Association while working in account management positions with Burson Marsteller and Weber Shandwick Worldwide. She holds a Bachelor of Science degree in Public Relations from the University of Florida and was a member of the Golden Key National Honor Society.

KEY MESSAGES ON COGNITIVE AGING, COGNITIVE DECLINE AND MEMORY LOSS DUE TO AGING

Developed and Approved, April 2019 for use by McKnight Brain Institute Leadership and Researchers and Individuals Speaking on behalf of the McKnight Brain Research Foundation

Overview

The following key messages were developed by the Communications Working Group, reviewed by the Leadership Council, and endorsed by the McKnight Brain Research Foundation (MBRF) Board of Trustees in April of 2019. The messages are meant as the foundation to build a common language the researchers across the four McKnight Brain Institutes and McKnight Brain Research Foundations Trustees can use to describe key concepts and terms. The messages are not meant to be prescriptive or limiting in any way, but are intended as a starting point to help with discussions with the public or with media.

We envision that these messages will be used by spokespeople representing the McKnight Brain Research Foundation and McKnight Brain Institutes to help raise the level of public awareness about cognitive aging and age-related memory loss. Considering recent scientific advances, there is growing evidence that cognition and brain health can be maintained throughout life. Using the messages below in a consistent manner will help the McKnight network of experts share information with the public in a relatable, engaging manner. The messages are meant as a guide to help convey consistent points across interviews and should be customized and expanded as needed.

1. What is Cognitive Aging?

Three proposed scientific summary statements:

- Cognitive aging refers to the effect age has on cognition.
- The effects, and therefore impact, of cognitive aging are not uniform. *They can involve one cognitive domain (e.g., memory), or another (e.g., processing speed.) They may impact a person in subtle ways that can be annoying, like not instantly finding the right word, or forgetting where you put your glasses.*
- Cognitive aging is NOT defined by a neurological or psychiatric disease or process.

Proposed key messages in lay terms:

- As we age, our brains age too.
  - Cognitive aging is a natural process that can have both positive and negative effects.
  - These effects vary widely from person to person.
- Our brains age at different rates and in different ways.
  - While wisdom, expertise and vocabulary increase with age, other abilities like processing speed, decision-making and some types of memory may decline with age.
- Cognitive aging is not a disease.
  - The brain changes associated with aging are part of a natural process that starts at birth and continues throughout the lifespan.
- With behavioral and lifestyle changes, there is increasing evidence that cognition and brain health can be maintained.

2. What is Successful Aging?

Proposed scientific summary statement about what activities or behaviors could maintain brain and cognitive health throughout life and help delay or minimize the negative effects of cognitive aging:

- Cognitive training and increased physical activity are interventions that have encouraging, although inconclusive, evidence in delaying or slowing age-related cognitive decline. (*Cognitive training is defined as a broad set of interventions, such as those aimed at enhancing reasoning, memory, and speed of processing".*)[1]

Proposed key messages in lay terms:

- Successful aging is normal brain aging without changes in memory or thinking skills that affect activities of daily living.

- Research suggests there are steps you can take to age successfully and maintain brain health as you age, including:
  - Staying physically active;
  - Reducing and managing your risk for cardiovascular diseases by managing your blood pressure, weight, and cholesterol levels;
  - Regularly discussing with family members any noticeable changes in your cognitive abilities or memory. Ask them to tell you and your doctor about the changes they may have noticed;
  - Regularly reviewing with your physician the health conditions you have and the medications and supplements you take that may impact your cognitive health;
  - Staying socially and intellectually engaged; and
  - Getting the recommended amount of sleep.

3. Importance of Cognitive Health Assessments/Steps to Minimize Risk

Scientific summary statements:

- Cognitive aging is not easily defined by clear thresholds on cognitive tests since many factors, including culture, occupation, education, environmental context and health variables (medications, depression) influence test performance and norms.
- For an individual, cognitive performance is best assessed at several points in time.
- The changes that happen with aging are usually so subtle that it's hard to test for them other than with sequential evaluation and advanced neurological tests.

Proposed key messages in lay terms:

- Changes with your brain health happen slowly over time and aren't always easy to detect. Changes in your ability to process, learn or remember can be caused by stress, depression, loneliness, hearing and vision loss, and financial problems, among other difficulties.
- Be sure to talk with your family and your healthcare providers about any memory changes you notice or concerns you have, and ask if you should undergo a cognitive assessment.
- It's never too soon or too late to protect your brain health. Taking steps now, like staying physically active, getting enough sleep and reducing and managing your risk for cardiovascular disease can help minimize the effects of cognitive aging and help you age successfully.
- Because aging happens over a lifetime, it is good to encourage younger people to pay attention to the things that will help them to age successfully.

[1] National Academies of Sciences, E., et al., in *Preventing Cognitive Decline and Dementia: A Way Forward*, A. Downey, et al., Editors. 2017, National Academies Press (US)

4. Cost Associated with Cognitive Aging and Memory Loss/Prevalence

Given the lack of data quantifying the number of people affected by cognitive aging and the associated cost, the statistics below can be used to help frame the issue in terms of prevalence and concern.

"The 87%", The Journals of Gerontology, Series A, Vol 67, Issue 7, July 2012 - Molly V. Wagster, PhD, et al

- One in eight people 65 and older (13 percent) develops Alzheimer's disease.
- The remaining 87 percent are experiencing cognitive changes attributable to the normal aging process to varying degrees.

AARP 2016 Member Opinion Survey Results

- 84 percent of members surveyed (age 50 and older) were very concerned with staying mentally sharp.
- Staying mentally sharp (90 percent) and physically fit (87 percent) were the top two health/self-related interests among those surveyed.

Cognitive Aging Explained

McKNIGHT BRAIN RESEARCH FOUNDATION

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What is Cognitive Aging?

As we age, our brains age too. Cognitive aging is a natural process that can have both positive and negative effects and these effects vary widely from person to person.

Our brains age at different rates and in different ways. While wisdom, expertise and vocabulary increase with age, other abilities like processing speed, decision-making and some types of memory may decline with age.

Did You Know?

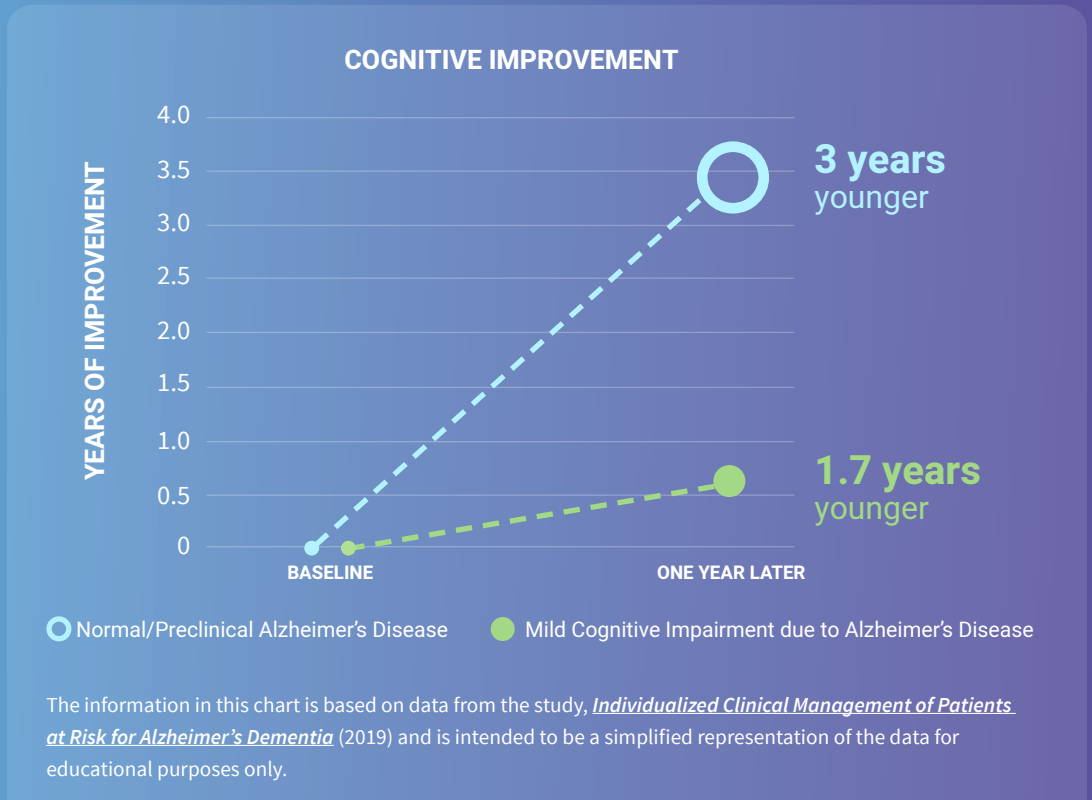
Cognitive health is the ability to clearly think, learn and remember. It's just one component of overall brain health and is an important component of performing everyday activities.

The research and information offered by the McKnight Brain Research Foundation are intended only for educational purposes and not to serve as medical or pharmaceutical advice.

Cognitive Aging Is Not a Disease

The brain changes associated with aging are part of a natural process that starts at birth and continues throughout the lifespan. Cognitive aging cannot be prevented, but there are steps you can take to optimize your brain and cognitive health.

Recent research found that adopting a series of lifestyle changes such as diet, exercise and challenging your brain by learning a new skill or starting a new hobby, helped people maintain and even improve their memory. The study examined the effects of individualized clinical management among people at risk for cognitive decline in a real-world clinic setting.



The information in this chart is based on data from the study, ***Individualized Clinical Management of Patients at Risk for Alzheimer's Dementia*** (2019) and is intended to be a simplified representation of the data for educational purposes only.

On average, after one year in the study, the cognitive function of a person with mild cognitive impairment (MCI) due to Alzheimer's disease looked like that of a person 1.7 years younger, and the cognitive function of someone with normal memory or preclinical Alzheimer's disease (i.e. exhibiting no evidence of cognitive impairment) looked like that of a person 3 years younger.

Optimizing Cognitive Health

A growing body of scientific research suggests the following factors promote cognitive health as you age:

Maintain your physical health.

- Get health screenings as recommended for your age.
- Talk with your doctor about the medicines you take and discuss the possible side effects they may have on your memory, sleep and brain function.
- Don't smoke or use other nicotine products.
- Get enough sleep – aiming for 7-8 hours every night.

Manage high blood pressure and other vascular conditions.

- Preventing or controlling high blood pressure may help your brain in addition to your heart.
- Observational studies have shown having high blood pressure in midlife – from your 40's to early 60's – increases the risk of cognitive decline later in life.

Keep your mind active.

- Staying intellectually engaged is one of the most powerful things you can do to maintain brain health.
- Reading books; playing games, like chess; solving crosswords; or learning a new skill, like a foreign language or photography can reduce your risk of developing cognitive impairment.

Eat healthy foods.

- Eating a healthy diet with a variety of fruits and vegetables, whole grains, lean meats, fish, poultry, and low-fat or nonfat dairy products can reduce the risk of many chronic diseases and promote brain health.

Engage in physical activity.

- Physical activity is beneficial for the brain and cognition.
- Aim for 30 minutes of physical activity every day.

Stay connected.

- Connecting with people through social activities and community programs may improve cognition and lower the risk of other health problems. It also helps improve mood and psychological functioning.

Manage stress and other mental health conditions.

- Stress is a natural part of life, but over time, chronic stress can negatively impact the brain, affect memory, and increase the risk for Alzheimer's and related dementia.
- Manage stress by getting help from a counselor or therapist, reaching out to friends and family for support, writing in a journal, and practicing relaxation techniques.

Memory & Aging

As you get older, it's normal to worry about your memory and thinking abilities. These changes are usually associated with mild forgetfulness – often a normal part of aging – and not a sign of a serious memory problem.

Know the Difference

Some normal signs of aging include:

- Making a bad decision once in a while
- Missing a monthly payment
- Losing track of time
- Not being able to find the right words
- Losing things around the house

Serious memory problems make it hard to do everyday things like driving and shopping. Signs may include:

- Asking the same questions repeatedly
- Getting lost in familiar places
- Inability to follow instructions or directions
- Becoming confused about time, people, and places

If you or a loved one is experiencing signs of a serious memory problem, talk with a doctor to determine whether the memory problems are normal and to find out what may be causing them.

Memory and other thinking problems have many possible causes, including depression, an infection, or medication side effects. Sometimes, the problem can be treated, and cognition improves. Other times, the problem is a brain disorder, such as Alzheimer's disease, which cannot be reversed.

Diagnosing

Talk to your doctor about any of the memory problems you're experiencing. Finding the cause of your memory problems is an important first step in determining the best course of action to address them.

ABOUT THE MCKNIGHT BRAIN RESEARCH FOUNDATION

The McKnight Brain Research Foundation is the only private foundation devoted exclusively to solving the mysteries of the aging brain and helping people achieve a lifetime of cognitive health.

Our Strategic Pillars

Lead

First to establish a dedicated area of research specifically focused on age-related cognitive decline and memory loss

Inspire

Sharing information and research to help people maintain cognition and brain health for life

Partner

Forming partnerships and collaborations among scientists, institutions and organizations

Recognize & Reward

Offering scholarships and grants to attract bright young researchers and support current scientists

The McKnight Impact

$180,000,000

Funding over $180 million in research specifically targeting cognitive aging, age-related cognitive decline and memory loss through direct contributions and strategic initiatives in partnership with the four McKnight Brain Institutes and the National Institute on Aging (NIA) through the Foundation for the National Institutes of Health (FNIH)

240+

Researchers and five endowed Chairs supported across the four McKnight Brain Institutes

$15M

Awarded to FNIH - resulting in nearly 40 new grants over two cycles

10 scholars

Partnering with the **American Academy of Neurology** via the **American Brain Foundation** to fund ten cognitive aging research scholarships over five years

4 institutes

Established McKnight Brain Institutes at the University of Alabama at Birmingham, the University of Arizona, the University of Miami and the University of Florida

3 summits

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1 report

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Keeping Your Brain Healthy

Brain Health Facts

It's a fact: your brain ages just like the rest of your body. It shrinks in size, slows down in speed, and becomes less adaptable to change as you age. While research on how to maintain brain health later in life continues at a rapid and expanding pace, we know there is growing hope and expectation that living longer, fuller cognitive lives is possible.

Brain health refers to how well your brain functions across several areas. Aspects of brain health include:

Cognitive Health

How well you think, learn and remember.

Motor Function

How well you make and control your movements, including balance.

Emotional Function

How well you interpret and respond to emotions – both pleasant and unpleasant.

Tactile Function

How well you feel and respond to sensations of touch, including pleasure, pain and temperature.

Tips to Maintaining Brain Health

Growing evidence shows that making behavioral and lifestyle changes can help you maintain cognition and brain health later in life.

Adopting a combination of healthy behaviors, which have also been shown to reduce cancer, diabetes and heart disease, will help you achieve maximum benefits for both your brain and body. And the good news is, **it's never too late** to adopt healthy habits.

Did You Know?

Brain health can be affected by age-related changes in the brain; injuries, such as stroke or traumatic brain injury; mood disorders, like depression, substance abuse or addiction; and diseases, like Alzheimer's disease.

Strategies to Protect Brain Health

Start adopting these 8 strategies today to protect your brain health now and in the future:

Exercise

Break a sweat and engage in regular cardiovascular exercise that elevates the heart rate and increases blood flow to the brain and body. Several studies have linked regular physical activity with a reduced risk of cognitive decline.

Quit Smoking

Evidence shows that smoking increases risk of cognitive decline. Quitting smoking can reduce that risk to levels comparable to those who have not smoked.

Get Enough Sleep

Not getting enough sleep may result in problems with memory and thinking, yet a third of American adults report regularly getting less than the recommended 7-8 hours of sleep. Help protect your brain by getting better sleep.

Stay Socially Engaged

Social and intellectual engagement is important to brain health. Pursuing interesting and meaningful social activities will help you keep connections with others. Try volunteering at a local church or animal shelter or just share the activities you enjoy with friends and family.

Keep a Healthy Heart

The risk factors for cardiovascular disease and stroke — obesity, high blood pressure and diabetes — also have been shown to negatively impact cognitive health. Preventing and managing high blood pressure and cholesterol will help protect the heart and take care of the brain.

Eat a Healthy and Balanced Diet

Following a diet that's low in fat and high in vegetables and fruit has also been linked to reducing the risk of cognitive decline. Although research on diet and cognitive function is limited, certain diets, like the Mediterranean and Mediterranean-DASH (Dietary Approaches to Stop Hypertension), may help maintain brain health.

Continue Learning and Welcome Challenges

Challenging and activating the mind by doing puzzles, building furniture or playing games are good ways to encourage strategic thinking. Taking an online class or learning a new language will also help keep your mind sharp.

Don't Forget Mental Health

Some studies also link depression with increased risk of cognitive decline. Managing stress and seeking medical attention for any symptoms of depression, anxiety or any other mental health concerns will help optimize your brain health.

Exercise for Brain Health

Did You Know?

Exercise is linked to stimulating the brain's ability to maintain and create network connections – which is linked to improvements in memory, learning, and spatial memory.

Physical activity is a valuable part of any overall body wellness plan and is associated with a lower risk of cognitive decline.

Many recent studies have linked regular physical activity with benefits for the brain. In fact, exercise has been linked to stimulating the brain's ability to maintain old network connections and make new ones that are vital to cognitive health, as well as increasing the size of a brain structure important to memory and learning and improving spatial memory.

Beneficial Exercises

Be sure to consult a doctor about your overall health before starting any new exercise program.

Aerobic Exercise

Aerobic exercise, such as brisk walking, is thought to be more beneficial to cognitive health than non-aerobic stretching and toning exercise. Research is ongoing, but aiming to move for about **30 minutes** on most days is shown to have many benefits.

Cardiovascular Exercise

Engage in cardiovascular exercise to elevate your heart rate, if you're able to do so safely. This will increase the blood flow to the brain and body, providing additional nourishment while reducing potential dementia risk factors like high blood pressure, diabetes and high cholesterol.

The More The Merrier

Incorporating other physical activities you may enjoy, like walking with a friend, taking a dance class, joining an exercise group or golfing may also be mentally or socially engaging. Activities can be as simple as bike riding, gardening or walking the dog.

Tips to a Brain Healthy Diet

Many foods, including blueberries, leafy greens, and curcumin (found in the spice turmeric), have been studied for their potential cognitive benefit. These foods were thought to have anti-inflammatory, antioxidant or other properties that might help protect the brain. So far, there is no evidence proving that eating or avoiding a specific food can prevent age-related cognitive decline.

While research on the relationship between diet and cognitive function is somewhat limited, it does point to the benefits of two specific diets that can reduce heart disease and may also be able to reduce the risk of cognitive decline: the DASH (Dietary Approaches to Stop Hypertension) diet and the Mediterranean diet.

The Dietary Approach to Stop Hypertension (DASH)

The DASH diet aims to reduce blood pressure and recommends:

Eating a diet that is low in saturated fat, total fat and cholesterol; and high in fruits, vegetables and low-fat dairy.

Consuming whole grain, poultry, fish and nuts.

Decreasing intake of fats, red meats, sweets, sugared beverages and sodium.

The Mediterranean Diet

The Mediterranean Diet incorporates different principles of healthy eating, typically found in the areas bordering the Mediterranean Sea and recommends:

Focusing on fruit, vegetables, nuts, and grains.

Replacing butter with healthy fats, like olive oil.

Limiting red meat.

Using herbs to flavor food instead of salt.

Eating fish and poultry at least twice a week.

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Top 10 Tips for

Healthy Aging

We celebrated Healthy Aging Month in September by sharing tips and encouraging you to take action to prioritize your brain health. Whether you joined us in September, or are looking to make changes now to promote healthy aging and good brain health, the top 10 tips below will help jumpstart your new lifestyle.

Top 10 Tips for Healthy Aging

Practice Healthy Eating Habits

Having breakfast and healthy snacks, like fruits or nuts, throughout the day may help improve your memory function.

Get Active

Break a sweat! Physical activity is crucial to your brain health.

Get Enough Sleep

Aim to get the 7-8 hours a night recommended for adults.

Stay Connected

Stay engaged socially to help maintain cognition and protect your brain health.

Mind Your Meds

Be sure to consult with your doctor before starting any new medications.

See Your Doctor Regularly

Keep up with regular doctor's appointments and stay on top of health screenings.

Keep Your Heart Healthy

Preventing and managing high blood pressure and cholesterol helps protect your heart and your brain.

Take a Deep Breath, Meditation is Good for You

Meditation can help improve anxiety and depression, so squeeze in some TLC time. Your brain will thank you!

Stay Hydrated

Just like the rest of your body, your brain benefits from getting the recommended water intake.

Learn New Things

Challenge and activate your mind by trying new activities or learning a new skill or language.

Keep Your Brain Healthy

Read our new *Keeping Your Brain Healthy* brochure and start making changes to keep your brain healthy today.

Read the Brochure

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The McKnight Brain Research Foundation

Championing research to better understand and alleviate the effects of age-related cognitive decline and memory loss since 1999.

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The McKnight Brain Research Foundation and four McKnight Brain Institutes foster cross-discipline, productive collaboration among leading researchers to better understand and alleviate the effects of age-related cognitive decline and memory loss.

The scientific research conducted at the McKnight Brain Institutes examines the fundamental mechanisms that underlie the neurobiology of learning and memory and the influences contributing to successful aging. Findings and discoveries are applied clinically to help people maintain their cognitive health and manage the effects of age-related cognitive decline and memory loss.

In the photo: McKnight Brain Institutes' Leadership Council (L-R) Lee Ryan, Ph.D. (UA); Thomas Foster, Ph.D. (UF); Ron Lazar, M.D. (UAB); Todd Golde, M.D.; Ph.D. (UF); Steven DeKosky, M.D.(UF); Carol Barnes, Ph.D. (UA); Ralph Sacco, M.D. (UM); Ronald Cohen, Ph.D. (UF); and Tatjana Rundek M.D., Ph.D. (UM). Not pictured: David G. Standaert, M.D., Ph.D. (UAB), Erik D. Roberson, M.D., Ph.D. (UAB) and Jada Lewis, Ph.D. (UF).

Evelyn F. McKnight Endowed Chairs

Recognizing Evelyn McKnight's generous support for ongoing brain research, the McKnight Brain Research Foundation established Endowed Chairs at each of the four McKnight Brain Institutes in her honor.

- Evelyn F. McKnight Endowed Chair in the Department of Neurology at the University of Alabama at Birmingham
- Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging at the University of Arizona
- Evelyn F. McKnight Chair for Research on Cognitive Aging and Memory and Evelyn F. McKnight Chair for Clinical Translational Research in Cognitive Aging at the University of Florida
- Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging at the University of Miami

The University of Alabama at Birmingham

Established in 2004, the Evelyn F. McKnight Brain Institute at the University of Alabama at Birmingham (UAB) brings together scholars and researchers working in the forefront of basic, translational and clinical neuroscience, with the overarching goals of discovering new biological principles in pre-clinical models and bringing them to bear on human cognitive concerns.

Utilizing state of the art laboratory facilities, brain imaging modalities, and clinical settings, the UAB MBI faculty and students explore the mechanisms that underlie human and animal cognitive neuroscience in an effort to develop new interventions for creating cognitive resilience as people age.

Evelyn F. McKnight Brain Institute Leadership

Director, Ronald M. Lazar, Ph.D., FAHA, FAAN

Director and Evelyn F. McKnight Endowed Chair, Dr. Ronald M. Lazar, is a graduate of New York University with a prize in Psychology and a PhD graduate in Psychology from Northeastern University. Since beginning his tenure with UAB, Dr. Lazar has worked to fulfill his vision of establishing new relationships with patient-oriented departments and clinical faculty to build upon the already-existing strengths in basic and translational neuroscience at UAB.

Associate Director, Kristina Visscher, Ph.D.

Associate Director, Dr. Visscher received her Ph.D, in Biological and Biomedical Sciences from Washington University in St. Louis and completed postdoctoral positions at Brandeis and Harvard Universities before joining the UAB faculty in 2009. Dr. Visscher is an Associate Professor in the UAB Department of Neurobiology and her research interests in cognitive neuroscience include investigating how the human brain can process the same environmental inputs in different ways at different time points

Learn More About the Leadership Team on the UAB MBI Website →

Specialized Research on Cognitive Aging

Research at the UAB McKnight Brain Institute involves an interdisciplinary collaboration across departments and programs at the University of Alabama Birmingham, targeted at mitigating age-related cognitive decline.

McKnight Brain Aging Registry (MBAR)

With tremendous investment in organizing and harmonizing data from across the four McKnight Brain Institutes, the McKnight Brain Aging Registry now includes a single data set that has undergone quality control and is sufficiently similar to be compared across sites. Recruitment and data acquisition for this collaborative project remains in progress.

Clinical and Population-based Research

Clinical and population-based research at the UAB MBI focuses on healthy aging adults, as well as adults with age- related memory loss and cognitive decline, dementia, stroke and other cerebrovascular conditions, among others. Areas of research include: cognitive resilience and recovery in aging; age-related cognitive function; quality of life for the aging through research, education and clinical care; functional activity, decisional capacity, and cognition in persons with cognitive impairment; and more.

Center for Translational Research on Aging and Mobility

The Center for Translational Research on Aging and Mobility is a multisite study measuring cognitive testing and brain MRIs.

55+
faculty members spanning across more than 15 academic departments

200+
peer reviewed publications in high impact journals annually

Learn more about the UAB MBI →

The University of Arizona

Founded in 2006, the mission of the Evelyn F. McKnight Brain Institute at the University of Arizona is to discover the mysteries of the normally aging brain to achieve a lifetime of cognitive health.

Scientists used to view the aging brain as an inevitable story of decline. It's now known that the brain continually adapts throughout life— a more hopeful outlook on the world's most condensed mystery.

Because of the inventive research of Dr. Carol Barnes and other affiliated faculty, along with the continual development of new technologies, the Evelyn F. McKnight Brain Institute is poised to contribute to southern Arizona as a center for high-level neuroscience, while also improving the understanding of brain and cognitive health for the entire world.

Evelyn F. McKnight Brain Institute Leadership

Director, Carol A. Barnes, Ph.D.

Director, Dr. Carol A. Barnes is a Regents Professor in the Departments of Psychology, Neurology and Neuroscience, the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging, Director of the Evelyn F. McKnight Brain Institute and Director of the Division of Neural Systems, Memory & Aging at the University of Arizona, Tucson, Arizona. Dr. Barnes is past-president of the Society for Neuroscience, an elected Fellow of the American Association for the Advancement of Science, and an Elected Foreign Member of the Royal Norwegian Society of Sciences and Letters, and an elected fellow of the National Academy of Sciences.

Associate Director, Lee Ryan, Ph.D

Dr. Lee Ryan is a Professor in the Departments of Psychology and Neuroscience, Associate Director of the Evelyn F. McKnight Brain Institute, Director of the Cognition and Neuroimaging Laboratory, Head of the Department of Psychology at the University of Arizona, Tucson, Arizona. Her work focuses on investigating the aging brain and how memory changes with age to identify ways to maintain a healthy brain through healthy lifestyle choices.

Learn More About the Leadership Team on the UA MBI Website →

Research on the Neurobiology of Cognitive Aging

The investigators at the Evelyn F. McKnight Brain Institute at the University of Arizona gain insights into brain function and cognition during aging using multiple animal models that include flies, rodents and nonhuman primates, as well as human participants. Institute investigators use cutting-edge and specialized behavioral assessments specifically created to be sensitive to those cognitive domains that change during normative aging, including tests for humans, as well as tests for the animal models of aging investigated.

Methods applied to understanding the mechanisms of brain aging that underly cognitive change with aging include state-of-the-art ensemble electrophysiological recording in behaving animals that can monitor changes in brain networks and cognitive decline in aged rodents and nonhuman primates and can be combined with live imaging methodologies. Other large-scale molecular imaging technologies are also used (the catFISH method) that allow the examination of individual cells that participate in circuits critical for memory. Genetic, proteomic and epigenetic methods are also used by the EMBI researchers at the University of Arizona, and, in collaboration with our colleagues at the other McKnight Brain Institutes, to understand changes in molecular pathways that control cell function and are critical for brain plasticity mechanisms. The Evelyn F. McKnight Brain Institute in Tucson also shares and develops sophisticated methods for collection of functional and structural MRI data in humans, and is a leader in developing machine learning and other advanced approaches for analyses of these data.

40+

affiliate faculty spanning 21 departments and 5 colleges

200+

articles published annually on topics related to aging

$29M

in research funding

Learn more about the UA MBI →

The University of Florida

With the start of the new millennium, the University of Florida Brain Institute, a world class $60 million building, was renamed the Evelyn F. and William L. McKnight Brain Institute of the University of Florida (UF MBI) to celebrate and commemorate a **$15 million** gift from the McKnight Brain Research Foundation.

Today, the UF MBI is one of the nation's most diverse neuroscience research centers. Its mission extends far beyond its physical walls and serves as a "transparent umbrella" connecting and supporting faculty members from other departments, centers and programs with concentrations in neuroscience research throughout UF's 16 colleges. Across campus, researchers collaborate with cognitive aging core faculty — supported by the gift from the McKnight Brain Research Foundation — on multidisciplinary teams to better understand how the brain works and how various diseases alter brain function.

Ultimately these researchers and physician-scientists hope to broaden the understanding of many neurological and psychiatric disorders and change them from untreatable to treatable, incurable to curable and inevitable to preventable.

Evelyn F. & William L. McKnight Brain Research Foundation Leadership

Director, Jennifer L. Bizon, Ph.D.

Dr. Jennifer Bizon is a Professor and Chair of the Department of Neuroscience and Director of the Eveyln F. and William L. McKnight Brain Institute. Her research program is broadly focused on understanding brain aging and its implications for cognitive function. Dr. Bizon received her Bachelor of Science degree from the University of North Carolina at Chapel Hill and Ph.D. from University of California, Irvine. Prior to joining the University of Florida, she received postdoctoral training at Johns Hopkins University and established her own laboratory at Texas A&M University.

Deputy Director, Steven T. DeKosky, M.D.

Steven T. DeKosky, M.D., is also the Aerts-Cosper Professor of Alzheimer's Research at the UF College of Medicine, co-deputy director of the UF MBI and associate director of the 1Florida ADRC. DeKosky earned the Alzheimer Association's Lifetime Achievement Henry Wisniewski Award in 2020.

Deputy Director, Jada Lewis, Ph.D.

Jada Lewis, Ph.D., is a professor of neuroscience and investigator at UF's Center for Translational Research in Neurodegenerative Disease. She has co-led the UF MBI's Education and Outreach Committee with Jennifer Bizon, Ph.D., for the last two-plus years.

Deputy Director, Gordon Mitchell, Ph.D.

Dr. Mitchell joined the University of Florida in 2015 as a Preeminence Professor of Neuroscience in the Department of Physical Therapy and McKnight Brain Institute. He opened and is Director of the UF Center for Breathing Research and Therapeutics (BREATHE) and an NIH-funded graduate and postdoctoral training program of the same name.

Evelyn F. McKnight Endowed Chairs for Research

Chair for Research on Cognitive Aging and Memory, Tom Foster, Ph.D.

Chair for Clinical Translational Research in Cognitive Aging, Ron Cohen, Ph.D., ABPP, ABCN

Learn More About the Leadership Team on the UF MBI Website →

Specialized Research on Cognitive Aging

Center for Cognitive Aging and Memory Clinical Translational Research (CAM Center)

Co-directed by Ron Cohen, Ph.D. ABPP, and Jennifer Bizon, Ph.D., with Sara Burke, Ph.D., and Adam Woods, Ph.D., serving as associate directors, the CAM Center is a multidisciplinary research center focused on brain aging and cognition with researchers specializing in physiology, neurobiology of aging, neuroplasticity, pharmacology, computational, cellular and behavioral neuroscience and clinical interests. Research approaches underway at the CAM Center include analysis of single cells and molecules; interrogation of neural circuits; and design and testing of interventions to improve cognitive health.

With strengths in both preclinical discovery-based research and clinical science, CAM Center researchers are dedicated to translating leading edge brain aging discoveries into interventions that will preserve cognitive function and improve the quality of lives for older adults. The CAM Center is a fertile training ground for those interested in preclinical or translational research careers focused on preventing or reversing age-related cognitive decline.

Learn more about the CAM Center →

200+

faculty members from more than 50 academic departments

3rd

ranking in neuroscience for NIH funding among public universities

50+

labs totaling 260,000 square feet of research space

Learn more about the UF MBI →

The University of Miami

Research at the Evelyn F. McKnight Brain Institute at the University of Miami is dedicated to advancing medical knowledge about memory loss and related neurological diseases.

UM MBI researchers are studying ways to improve the lives of people with Alzheimer's disease and other types of dementia, with a goal of developing new strategies to stop the disease process, minimize the impact on individuals, restore lost functions and eventually find the cause and cure for these devastating illnesses.

Evelyn F. McKnight Brain Institute Leadership

Executive Director, Tatjana Rundek, M.D., Ph.D.

Scientific Director and Evelyn F. McKnight Chair for Learning and Memory in Aging, Dr. Tatjana Rundek is a Professor of Neurology, Epidemiology and Public Health with tenure, Vice Chair of Clinical Research, and Director of the Clinical Translational Research Division in the Department of Neurology of the University of Miami, Miller School of Medicine. She holds a secondary faculty appointment at the Department of Neurology at Columbia University in New York.

Learn More About the Leadership Team on the UM Website →

Cognitive Aging Research

The McKnight MRI Core and Neuropsychology Core Projects

The McKnight MRI Core and Neuropsychology Core Projects are collaborative core projects with other McKnight Brain Institutes involving ongoing research and collection of standardized brain MRIs and neuropsychological assessment data in patients with memory and cognitive loss.

Evelyn F. McKnight Brain Institute Cognitive Disorders Clinical and Biorepository Registry Collection

This comprehensive longitudinal database registry includes patients with age-related memory disorders and dementias. Participants are enrolled from the University of Miami Memory Disorders Clinic, a collaborative effort between Neurology and Psychiatry & Behavioral Sciences. The databank collects information on patient demographics, clinical assessments, medical history, genetic risk factors, imaging data and treatment modalities.

Identification of Biomarkers for Early Diagnosis of Cognitive Impairment in the Elderly

This ongoing study aims to identify new biomarkers that can be detected in participants who are at risk of developing dementia and/or who have cognitive impairment.

Evaluating Frailty as a Preventive Measure in Maintaining Quality of Life in Aging

This frailty research evaluates a clinical and community cohort of aging adults to determine their propensity towards being non-frail, pre-frail and frail, with the goal of early detection and prevention of frailty symptoms and clinical characteristics.

Analysis of Cognition in Patients with Memory Complaints

By analyzing patients with memory complaints, this research project examines questions related to the cognitive, psychological and biomedical variables associated with dementia and its subtypes, including demographics and risk factors that help identify predictive variables to improve the understanding of dementia and other memory disorders and their comorbidities.

1st

medical school in Florida, the Leonard M. Miller School of Medicine, founded in 1952

1962

Founding of the Department of Neurology, one of the oldest departments within the Miller School

100+

clinical and research faculty, with one of the largest neurology training programs

Learn more about the UM MBI →

Chair

Michael L. Dockery, MD
Charlotte, NC

Vice Chair

Madhav Thambisetty, MD, PhD
Ellicott City, MD

Chair Emeritus

J. Lee Dockery, MD
Gainesville, FL

Corporate Trustee

Melanie A. Cianciotto
Orlando, FL

Trustee

Patricia A. Boyle, PhD
La Grange, IL

Trustee

John E. Brady MD
Newport News, VA

Trustee

Allison Brashear, MD, MBA
Buffalo, NY

Trustee

Susan L. Pekarske, MD
Tucson, AZ

Executive Director

Angelika Schlanger, PhD
Parkland, FL

Evelyn F. McKnight, a nurse, established the Evelyn F. McKnight Brain Research Foundation® on May 26, 1999. Mrs. McKnight and her late husband, William L. McKnight, were interested in the effects of aging on memory. This interest inspired Mrs. McKnight to establish the Foundation as a legacy of support for brain research with the specific goal of better understanding and alleviating age-related cognitive decline and memory loss.

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MBRF Gift Agreements
with the
McKnight Brain Institutes

Gift Agreements McKnight Brain Institutes (MBIs)

6. Evelyn F. McKnight Brain Institutes

A. University of Alabama at Birmingham (UAB)

1. Gift Agreements:

a. May 1, 2004—Gift Agreement provided for a gift of $5 million from the MBRF to be matched by the UAB over a five-year period of time. The Purpose of the gift was to support research of the brain in the fundamental mechanisms of the aging brain that underlie the neurobiology of memory with clinical relevance to the problems of cognitive decline and age-related memory loss.

The agreement also:

- Established the Evelyn F. McKnight Brain Institute.
- Established an endowed professorship for learning and memory in aging valued at $500,000.
- Michael J. Friedlander, PhD, Chair of the Department of Neurobiology would occupy the endowed chair.

b. October 19, 2005—Gift Agreement amended as follows:

- The MBRF agreed to contribute an additional $1 million to convert the Endowed Professorship to the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging valued at $1.5 million.
- The UAB agreed to match the additional $1 million contribution.
- Specified the locations of the Evelyn F. McKnight Brain Institute would be the 9th, 10th and 11th floors of the newly constructed Shelby building.

c. August 3, 2009—Gift Agreement amended as follows:

- Create a permanent $10 million Endowment.
- MBRF and UAB **each** funded $5 million. ($1 million per year for five years).
- The MBRF and the UAB would each contribute $500,000 per year for two years in addition to the endowment funds for operational costs.

2. Directors and Endowed Chairs: Chair Value: $1.5 million
   a. Director and Chair: David J. Sweatt, PhD—2006-July 2016
   b. Interim Director: Dr. David Standaert, M.D. PhD—July 1-May 31, 2017
   c. Director and Chair: Ronald M. Lazar, PhD—June 1, 2017—present
   d. Associate Director: Eric Roberson, M.D., PhD October 1, 2015 —December 31, 2022
   e. Associate Director: Kristina Visscher, PhD—January 1, 2023--Present
   f. Chair, Advisory Committee for MBI at UAB—Dr. David Standaert, June 1, 2017--Present

B. University of Arizona (UA)

1. Gift Agreements:

a. October 17, 2006—Gift Agreement provided for a gift $5 million from the MBRF matched by the UA over a five-year period of time. The purpose for the gift was for the overall support of the research of the brain intended for clinical application to accomplish alleviation of age-related memory loss.

The agreement also:

- Established the Evelyn F. McKnight Brain Institute.
- Established the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging valued at $1 million.
- Named Carol A. Barnes, PhD, as the occupant of the endowed chair.

1.b. University of Arizona – Gift Agreements, Continued

b. July 10, 2008—Gift Agreement amended as follows:

- The MBRF agreed to contribute an additional $300,000 to recruit a departing research scientist critical to Dr. Barnes' research.

c. May 1, 2014—Gift Agreement amended as follows:

- Create a permanent $10 million Endowment.
- MBRF and UA each fund $1 million per year for five years.
- The MBRF and the UA would each contribute an $200,000 per year for three years in addition to the endowment funds for operational costs.
- Both parties agreed that if in any given year the match could not be made, funds in the amount equal to the amount which would-be due for distribution on the value of the endowment at that time would be contributed by the defaulting party and will be cumulative until the obligation is met.

2. Directors and Endowed Chairs: Chair Value: $1.0 million

a Director and Chair: Carol A. Barnes, PhD—2006—present

b. Associate Director: Lee Ryan, PhD—2014—present

C. University of Florida (UF)

1. Gift Agreements

a. April 28, 2000-- Gift Agreement provided for a gift of $15 million from the MBRF matched by the state of Florida over a five-year period of time through a matching program approved by the state legislature to create a permanent endowment.

The agreement also:

- Established the Evelyn F. and William L. McKnight Brain Institute (MBI) of the University of Florida.
- Established the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging valued at $4 million, ($2 million from the MBRF and $2 million from match).
- Established a $26 million McKnight Research Grant Fund ($13 million from the MBRF and $13 million match).
- The University agreed to fund the distribution of income for the McKnight Research Grant Fund as if the full match had been met, with decreasing commitments at the same rate as the increase in the level of match.

b. October 20, 2009-- Gift Agreement amended as follows:

- Established a Cognitive Aging and Memory Clinical Translational Research Program (CAM-CTRP) within the Institute on Aging at the UF.
- Divided the $3.2 million investment income from the McKnight Research Grant Fund and transferred one-half ($1.2 million) to the newly established Cognitive Aging and Memory Research Fund for support of the CAM-CTRP.
- It was agreed one-half of the investment income would be equally divided between the CAM-CTRP and the MBI to support research in cognitive aging and age-related memory loss.
- The UF agreed to a national search for a qualified clinical research scientist as a program director.
- Marco Pahor, M.D., Director of the Institute on Aging, would act as interim program director as well as the scientific director until the program director was recruited.

1. b. University of Florida – Gift Agreements, Continued

- July 1, 2010—Jennifer L. Bizon, PhD, was recruited as Associate Professor in the Department of Neuroscience and joined Thomas C. Foster, PhD, as a faculty member in the Age-Related Memory Loss Research Program in the MBI.
- October 3, 2011--The McKnight Research Grant Fund account was closed and the McKnight the endowment account was continued as the McKnight Cognitive Aging and Memory Research Fund.
- July 1, 2012—Ronald A. Cohen, PhD, a cognitive neuropsychologist, was recruited as the director of the CAM-CTRP.
- July 1, 2013—Adam J. Woods, PhD, was recruited as assistant professor in the CAM-CTRP.
- October 1, 2013—Sara Burke, PhD, and Andrew Maurer, PhD, were recruited to join the Age-Related Memory Loss research faculty in the MBI.

c. July 1, 2015-- Gift Agreement amended as follows:

- Established the Evelyn F. McKnight Endowed Chair for Clinical Translational Research in Cognitive Aging valued at $4 million.
- Funded the chair by taking $3 million from growth in the principle from the McKnight Cognitive Aging and Research Grant fund and $1 from the growth in the principal of Evelyn F. McKnight Endowed Chair Fund for brain Research in Memory Loss.
- Dr. Ron Cohen was named the occupant of the Evelyn F. McKnight Endowed Chair for Clinical Translational Research in Cognitive Aging.

d. November 11, 2016—Memorandum of Understanding amended the operation and management of the CAM-CTRP as follows:

- Transferred the CAM-CTRP from the Department of Geriatric Research on Aging at the Institute on Aging to the UF Department of Clinical and Health Psychology in College of Public Health and Human Performance.
- Transferred the three faculty members in the CAM-CTRP to the Department of Clinical and Health Psychology in the College of Public Health and Human Performance.
- Created a Center for Cognitive Aging and Memory Clinical Translational Research (The CAM Center).
- Renovated space in the McKnight Brain Institute for the location of the CAM Center.
- Continued the funding of the CAM-CTRP through the CAM Center via the equal division of the investment income from McKnight Cognitive Aging Research Grant Fund for continued funding of the Age-Related Memory Loss research programs in the MBI.

e. February 1, 2017--Amended and Restated Memorandum of Understanding dated Center for Cognitive Aging and Memory Clinical Translational Research (the CAM Center) was approved by the University of Florida.

- The CAM Center was located in space in the Evelyn F. and William L. McKnight Brain Institute and was identified as the Center serving all the colleges within the UF Health Science Center.
- Ronald A. Cohen, PhD, was named Director of the CAM Center.
- The funding for the CAM Center was for the CAM-CTRP which resided within the CAM Center under the direction of Dr. Cohen.

1.f. University of Florida – Gift Agreements, Continued

f. July 22, 2019—Jada Lewis, PhD professor in UF's department of neuroscience is appointed deputy co-director of the MBI

g. November 20,2022— The MOU dated November 11, 2016, was amended to move the Cognitive Aging and Memory Research Program primarily devoted to basic science research operating within the MBI to the Center for Cognitive Aging and Memory Clinical Translation Research along with the Cognitive Aging and Memory Clinical Translational Research Program (CAM-CTRP). See Schematic. November 11, 2016.

- Transfer the Age-Related Memory Loss (ARML) Core Program from the MBI-UF to the Center for Cognitive Aging and Clinical Translational Research (the CAM Center) as a collaborating partner with the Cognitive Aging and Memory Clinical Translational Research Program (CAM-CTRP) in the CAM Center.
- Name separate Co-Directors of the CAM Center for the administration of the ARML Core Program and the CAM-CTRP.
- Maintain the level of financial and infrastructure support through the CAM Center for the CAM-CTRP and the ARML Core Program currently in place.
- Develop complementary and collaborative research and educational programs between the ARML Core Program and the CAM-CTRP within the CAM Center intended to:
  1. Maintain and grow the research infrastructure for conducting cutting-edge discovery based cognitive aging research.
  2. Recruit, train and retain high-caliber young scientist interested in neural mechanisms for cognitive aging.
  3. Expand the scientific community at UF pursuing research relevant to age related cognitive decline and memory loss.
  4. Increase visibility of the research and develop messaging at local, national, and international level.
  5. Increase interactions and cohesion within the CAM Center, other UF Centers and industry partners to facilitate bidirectional (discovery to translation) cognitive aging and memory research at UF.
  6. Increase interactions with the other McKnight Brain Institutes and increase visibility of ARML Core Programs.
- Dr. Ron Cohen representing the CAM-CTRP and Dr. Jennifer Bizon representing the Age-Related Memory Loss research program in the MBI were named Co-Directors of the Center for Cognitive Aging and Clinical Translational Research (the CAM Center).
- Adam Woods, PhD, was named Assistant Director of the CAM-CTRP and Sara Burke, PhD, was named Assistant Director of the Cognitive Aging and Memory Program within the CAM Center

2. Directors and Endowed Chairs:
   a. Founding Executive Director: William G. Luttge, PhD—1995-1998 (Lectureship was funded in 2012)
   b. Executive Director: Todd E. Golde, MD, PhD—2016—July 31, 2022
   c. Interim Executive Director & Deputy Director: Steven T. DeKosky. M.D.—February, 2023
   d. Co-Deputy Director: Jada Lewis, PhD, 2019—present
   e. Director-Jennifer Bizon, PhD—Chair of the department of Neuroscience at UF was appointed Director of the MBI. February 2023.
   f. Steven T. DeKosky, MD remained Deputy Director of the MBI

2. University of Florida – Gift Agreements, Continued

g. Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging: (Valued at $4 million).
- Thomas C. Foster, PhD—2003—present

h. Evelyn F. McKnight Endowed Chair for Clinical Translational Research in Cognitive Aging: (Valued at $4 million). (Limited to five-year term, but renewable with mutual agreement, between MBRF and the UF).
- Ronald A. Cohen, PhD—2015—Renewed August 2020

g. Center for Cognitive Aging and Memory Clinical Translational Research (The CAM Center) Director, Ronald A. Cohen, PhD—2015— 2020
- Co-Director, Jennifer L. Bizon, PhD—2020—February 13, 2023 (When named Director of the MBI) (Age Related Memory Loss Program in CAM Center)
- Associate Director—Sara Burke, PhD—2020—March
- Co-Director, Sara Burke, PhD—March 7, 2023--Present
- Co-Director, Ronald A. Cohen, PhD—2020—present Clinical Translational Research Program in CAM Center
- Associate Director—Adam Woods, PhD—2020—Present

h. McKnight Brain Institute
- Director--Jennifer Bizon, PhD---February 12, 2023
- Associate Director—Steven T. Dekosky, MD—February 2023—Present
- Co- Director--Jada Lewis, Ph.D—February 2023--Present

D. University of Miami (UM)

1. Gift Agreements

a. December 24, 2006-- Gift Agreement provided for a gift of $5 million from the MBRF matched by the University of Miami (UM) over a five- year period of time. The agreement also:
- Established the Evelyn F. McKnight Center for Age-Related Memory Loss.
- The UM agreed to recruit, through a national search, a qualified research scientist as a scientific director.
- Created a Director of Education position who would be responsible for developing clinical and post graduate training programs in cognitive aging and age-related memory loss.
- The UM agreed to recruit a qualified individual to occupy the Director of Education position.

b. December 10, 2010—Name Changed from "Center" to the Evelyn F. McKnight Brain Institute at the University of Miami.

c. February 9, 2011—Memorandum of Understanding between the UM and the MBRF to which the UM agreed to contribute from other sources the amount of investment income which would have been distributed in each respective year until the match was completed by the UM. (Note: Match was completed by the UM in 2013)

d. December 2012 -- Richard Isaacson, MD, resigned as faculty member and director of the education program to become Director of the Alzheimer's Prevention Clinic and faculty member in the Department of Neurology at Weill Cornell Medicine and New York-Presbyterian Hospital.

1.e. University of Miami — Gift Agreements, Continued

e. December 2013 -- UM match obligation completed as defined in the 2002 Gift Agreement with gifts of $1.8 million from the Schoninger Family designated for memory and aging disorders and the Di Tuillo Trust in the amount of $400,000 for cognitive research.

f. August 22, 2014—Gift agreement amended as follows:

- Established the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging valued at $4 million, ($2 million from the MBRF and $2 million from UM).
- The MBRF funded the $2 million over three years, completing the gift in 2016.
- The UM match of $2 million was completed August 22, 2014.
- Clinton B. Wright, MD, the Scientific Director of the McKnight Brain Institute was named to occupy the endowed chair.
- Clinton Wright, MD, the scientific director of the Evelyn F. McKnight Brain Institute at the University of Miami was named the first Evelyn F. McKnight Chair.
- The $4 million-dollar endowed chair was funded with $2 million dollars from the UM or donors to be match by the MBRF with $2 million, funded over a two-year period concluding 9/30/2016
- August 22, 2014—University of Miami Completed its match requirement for funding the Evelyn F. McKnight Endowed Chair.

g. October 2014—Xiaoyan Sun, MD, Ph.D was named Director of Education

h. October 31, 2016—Dr. Clinton Wright resigned as Scientific Director of the Evelyn F. McKnight Brain Institute at the University of Miami.

i. October 31, 2016—Tatjana Rundek, MD, PhD was named Interim Scientific Director of the Evelyn F. McKnight Brain Institute at the University of Miami.

j. December 21, 2017—Dr. Tatjana Rundek, MD, PhD was named the Scientific Director of the Evelyn F. McKnight Brain Institute and Evelyn F. McKnight Chair for Learning and Memory in Aging at the University of Miami after a nationwide search.

k. October 31, 2018—Dr. Tatjana Rundek, MD, Ph.D was formally installed as the Evelyn F. McKnight Chair for Learning and Memory in Aging at the University of Miami with President Julio Frank, MD, PhD, MPH and Henri Ford, MD, MPH, Dean of the Miller Miami School of Medicine presiding with the trustees and colleagues in attendance.

l. October 23, 2019—The trustees approved proposal to fund the one-time funding in the amount of $200,000 to launch the *Evelyn F. McKnight Neurocognitive Post-Doctoral Fellowship*. The grant is for $100,000 annually for a period of two years for a total not to exceed $200,000.

m. October 28, 2021—The trustees approved one-time funding fund the *Evelyn F. McKnight Neurocognitive Clinical Scholar in Brain Health and Aging* postdoctoral training program in the amount of $250,000 to be matched by the University of Miami. The grant is for $50,000 annually for a period of five years for a total not to exceed $250,000 with the understanding recruitment for the scholars will be from a national qualified applicant pool and efforts would be made to retain the successful scholars as clinical science faculty.

1.n. University of Miami — Gift Agreements, Continued

n. May 1, 2022—James. E. Galvin, MD, MPH a renown neurologist with strong research interest in cognitive aging and memory disorders was appointed as the Chief of the Cognitive Aging Division and the Alexandria and Bernard Schoninger Endowed Chair in Memory Disorders. Dr. Galvin will also serve as Director Comprehensive Center for Brian Health in expanding the UM MBI clinical neurology and cognitive services

2. Directors and Endowed Chairs:
   a. Executive Director: Ralph Sacco, M.D.—2007—deceased, January 17, 2023*
   b. Scientific Director: Clinton B. Wright, M.D.—2007-2016
   c. Interim Scientific Director: Tatjana Rundek, M.D., PhD—2016—2018
   d. Scientific Director: Tatjana Rundek, M.D., PhD 2018—present*
   e. Evelyn F. McKnight Endowed Chair for Learning and Memory in the Aging:
      - Clinton B. Wright, M.D.— 2014-2016;
      - Tatjana Rundek, M.D., PhD 2018—present
   f. Alexandria and Bernard Schrodinger Endowed Chair in Memory Disorders.
      - James E. Galvin, MD, MPH—installed February 21, 2023

*With Dr. Sacco's impending death due to an aggressive brain cancer, Dr. Henri Ford, Dean of the Miami Miller School of Medicine appointed Dr. Rundek to occupy both the positions of Scientific Director and Interim Executive Director until the leadership of department of neurology could be identified since Dr. Sacco was also the Chair of the Department. With the approval of the MBRF the position of the Scientific Director will be abolished and Dr. Rundek will assume the position of Director of the MBI at UM with the appointment of an associator director when the leadership is established similar to the governance models of each of the other MBIs.

Exhibit I

McKnight Research Grant Fund Schematic

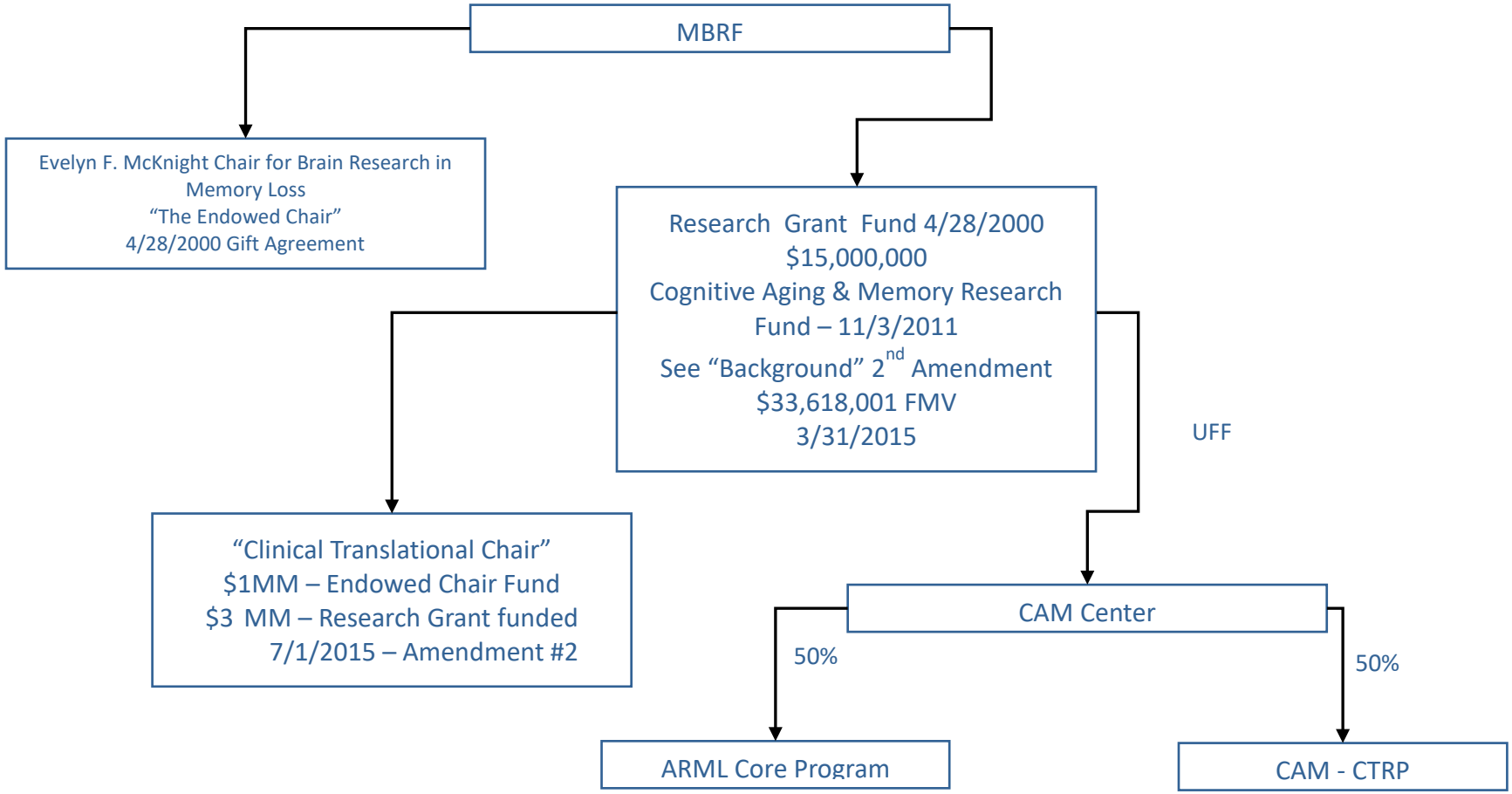


Exhibit II

McKnight Research Grant Fund Schematic

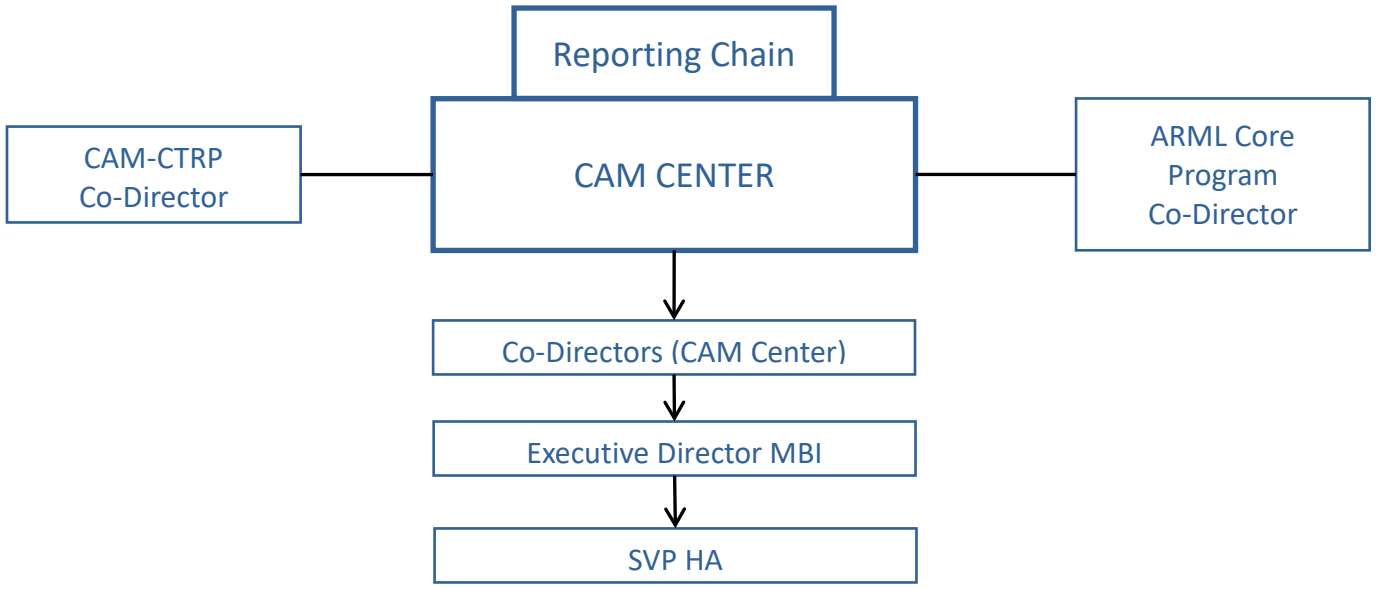
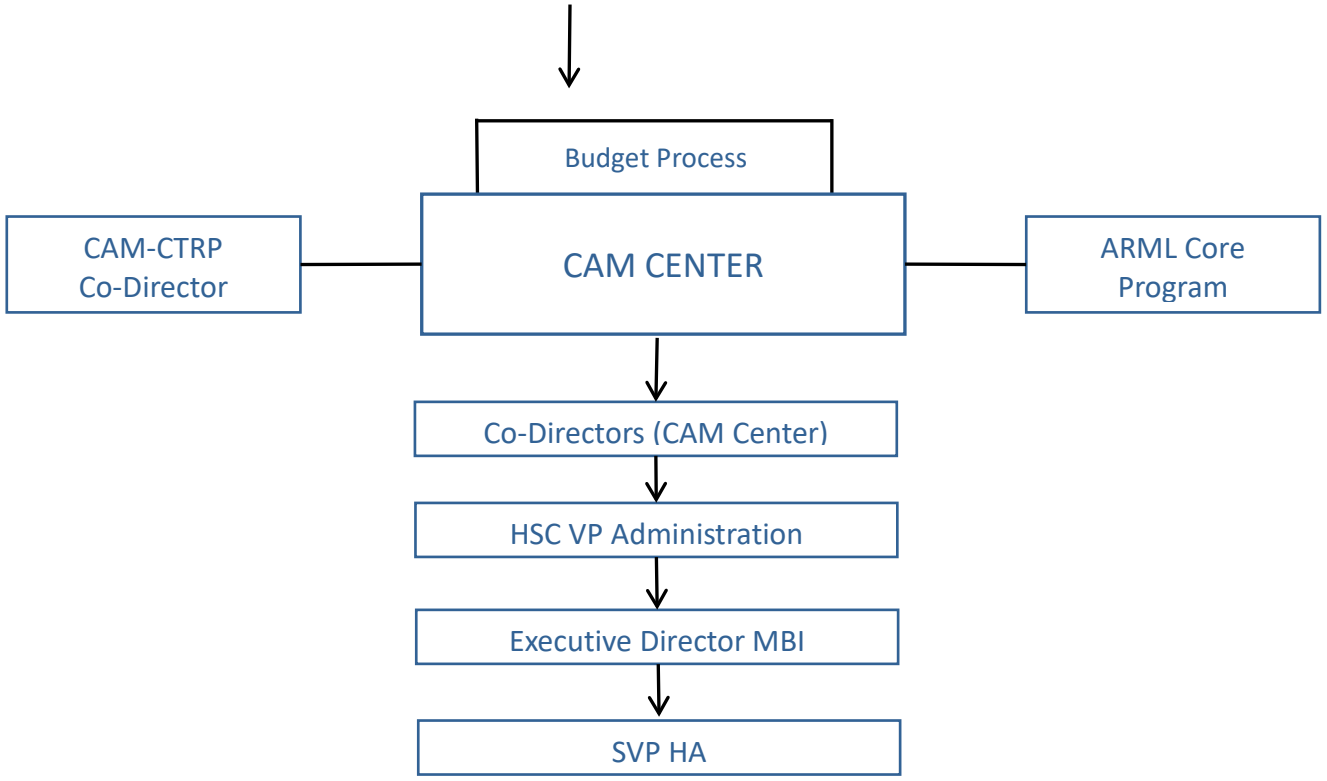


Exhibit III

McKnight Research Grant Fund Schematic



12/22/2016

McKnight Leadership Council
July 2023

Arizona

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cc: kbirwin@email.arizona.edu; fmorris@med.miami.edu; lbeasley@med.miami.edu; tstephens@uabmc.edu; calewi@uabmc.edu; cchambless@uabmc.edu; sabrina.sanchez@mbi.ufl.edu; tinalacy@ufl.edu; pjoy@ufl.edu; panolty@arizona.edu

McKnight Brain Research Foundation (MBRF)

Annual Report
Sponsored Institutes and Research Programs
(Include activity of all McKnight supported faculty and trainees)

Some gift agreements require Institute reports, Center Directors, and Chair reports.
If applicable, please clearly state whether a particular response relates to a Chair, Center or Institute.

Submitted by:_____

Report Period:_____

Please provide an easy to read, easy to evaluate summary of your MBI's activities, focusing on those that are new since last year's report. Please be succinct and focus on activities and accomplishments relevant to the McKnight Brain Research Foundation, i.e., age-related cognitive decline and memory loss. No item should be included in more than one section. Please spell out acronyms with first use when not universally understood.

1. Table of Contents

2. Letter from the Director(s). This signed and dated letter should summarize the current focus of the MBI, highlights and challenges of the past year, and major plans for the upcoming year.

3. Include a separate letter from each McKnight Chair, Center Director, or Chairholder if the Chairholder is not the Institute Director.

4. Institute FY21 at a Glance (Please include only items relevant to the MBRF's mission related to age-related cognitive decline and memory loss)

    - Summary of major scientific, programmatic, outreach or training achievements since last year, including clinical, translational programs, and educational programs

    - Identify and include what you consider the most important, relevant scientific achievement(s) of the past year

    - Provide the current MBI budget and an Endowment Investment Report

5. Collaborative Programs with McKnight Institutes and non-McKnight Institutes
   (Please reference any collaborative programs that are included in detail in Section 3. Please note, if the Principal Investigator of a collaborative study works within your MBI, please include an overview of the research being conducted in the collaborative study and include the names and affiliations of other collaborators.)

6. Honors, Awards and New Grants

7. Technology transfer (Patents/applications; Revenue generated from technology)

8. Were any funds used for a Prohibited Purpose during the report period?

9. Do you recommend any modification to the Purpose or mandates in the Gift Agreement?

10. Did all activities during the report period further the Purpose?

11. Additional Comments (items that are not covered elsewhere in the report, including any negative events, loss of full-time employees (FTEs), impending departures, space, or budget that could have an impact on carrying out the Gift Agreement.)

Signature (date, and title of person submitting the report)

Appendices

12. Appendix 1
    List of McKnight Affiliate Faculty and their area of focus, and Department Affiliations, including a list of post-doctoral and pre-doctoral trainees (CVs needed only for new faculty/collaborators)

13. Appendix 2
    Top 20 publications from FY21 relevant to the MBRF

14. Appendix 3
    Top 10 presentations at scientific or public meetings relevant to the MBRF

15. Appendix 4
    Highlights of website development, media coverage and/or social media audience development

PLEASE POST YOUR REPORT (EXCLUDING FINANCIAL INFORMATION) ON YOUR WEBSITE.

Annual Report

McKnight Brain Research Foundation
Sponsored Institutes and Research Programs
(Include activity of all McKnight supported faculty and trainees)
Report Period: _____

Financial Summary Format

_____(Institute)_____

Summary for 12 months ended _____

Account Name: _____

A.	Beginning Balance on _____	$ _____
B.	Investment Growth	$ _____
C.	Distributions	$ _____
D.	Additional Contribution	$ _____
E.	Ending Balance on _____	$ _____
F.	Unmatched Balance (if applicable)	$ _____

DEFINITIONS

DISTRIBUTION is the money transferred from the account to the spendable/operating account for the designated use.

BALANCE is the market value of the account as of the first or last day of the reporting year.

ADDITIONAL CONTRIBUTION is additional contribution by MBRF, the reporting institution, match etc.

INVESTMENT GROWTH (Loss) is the total undistributed interest, dividends, and realized and unrealized gains and losses.

BALANCE is the value of the account's corpus including all contributions, and applicable state match monies as of the date indicated.

MBRF Block Grants
and
Special Projects

McKnight Brain Research Foundation (MBRF) Block Grants, Pilot Grants and Special Projects

1. October 22, 2009—A Travel Award Program was approved by the MBRF Trustees. The Trustees established a travel award fund of $100,000 to support travel of research scientists to other McKnight Brain Institutes (MBIs) for educational purposes or to convene focus groups between MBIs to develop collaborative research programs.

2. 2012-2016—Cognitive Aging Core Working Groups were funded through the Travel Award Program. The five (5) working groups and their focus areas are as follows:

A. Brain and Cognitive Health Core Working Group
- Supports collaborative discussions to develop strategies to promote brain and cognitive health.

B. Cognitive Aging and Memory Interventional Core Working Group
- Supports collaborative discussions with the objective to accelerate clinical translation of interventions for alleviating cognitive aging and memory decline in older adults and to identify promising new cognitive aging interventions that could be rapidly implemented across the McKnight Brain Institute network and beyond.
- Supports the design, development, implementation and dissemination of multidisciplinary interventions for improved cognitive health as a necessary future direction.

C. Cognitive Testing Battery Core Working Group
Supports collaborative discussion on the adoption of common standards of cognitive tests which then would become common standards between investigators.

D. Epigenetics Core Working Group
- Supports discussions on development of a broad collaborative initiative to propel discovery and advancement concerning the role of epigenetic mechanisms and processes in memory and cognitive aging.

E. Magnetic Resonance Imaging (MRI) Standardization Core Working Group
- Supports collaborative working group to standardize the MRI data between the McKnight Brain Institutes and the calibration of the equipment at each MBI for consistency of results.

3. Several grants were funded by the MBRF Trustees after recommendation by the Core Working Groups. They are as follows:

A. September 1, 2013—Inter-Institutional Bio-Informatics Core--$600,000 ($300,000 for two years) funded upon recommendation by the Epigenetics Core Working Group. The two-year grant was approved to establish a comprehensive program to test an epigenetic hypothesis of cognitive aging, working collaboratively with all the McKnight Brain Institutes with the goal to establish a shared Inter-Institute resource to provide a catalyst for discoveries in the area of epigenetics of cognitive aging. This is envisioned to be a "core without walls" to provide support for bioinformatic analysis of high-throughput DNA/RNA sequencing and epigenomics, bioinformatics, and cross-correlation of human and animal studies.

- Principal Investigators:
  Dr. Matthew Huentleman, UA
  Dr. David K. Sweatt, replaced by Dr. Jeremy Day, UAB
  Dr. Tom Foster, UF

B. January 1, 2015—Inter-Institutional Neuroimaging Core--$931,759 (Two-year award) The two-year grant was approved upon recommendation by the MRI Standardization Core Working Group to establish and standardize a common neuroimaging protocol across all four McKnight Brain Institutes to develop a Cognitive Aging Assessment Core and a McKnight Brain Aging Registry of the oldest old. The purpose of the grant is to collect comprehensive data on brain morphology and function, cognition, and vascular risk, on participants 85 years and older, to support proposals for translational research to the NIH and other funding sources to identify and evaluate effective interventions for age related memory loss.

- Principal Investigators:
  Dr. Kristina Visscher, UAB
  Dr. Gene Alexander, UA
  Dr. Norm Halprin, UM
  Dr. Ron Cohen, UF

C. September 1, 2015--Inter-Institutional Cognitive Assessment and Brain Registry Core Award: $800,000 ($400,000 per year for two years) The funding request was approved upon the recommendation by the Brain and Cognitive Health Core Working Group. The purpose of the two-year grant is to establish and develop McKnight Cognitive Aging Assessment Core as a companion to the Inter-Institutional Neuroimaging Core to be provide supplemental cognitive testing to acquire comprehensive cognitive, behavioral, and relevant clinical data on older adults over the age of 85 to complete the Brain Aging Registry which would contain both the MRI and Cognitive assessment data.

- Principal Investigators:
  Dr Virginia G. Wadley, UAB
  Dr. Gene Alexander, UA
  Dr. Ron Cohen, UF
  Dr. Bonnie Levin, UM

4. July 16, 2016—The Trustees approved a proposal from the MBRF Clinical Translational Working Group to establish a "Cognitive Aging and Memory Intervention Core" without a budgetary requirement. The purpose of the Cognitive Aging and Memory Intervention Core is to create a high profile nationally recognized interventional hub for the four MBIs and to complement the existing Brain Aging Registry, Cognitive Assessment Core, and Epigenetics Core. The Cognitive Aging and Memory Intervention Core will identify research programs for collaborative potential between the four MBIs and solicit pilot grant proposals which would be reviewed by the Cognitive Aging and Memory Intervention Core. If approved by the core committee, the pilot grant proposal would be forwarded to the research committee of the MBRF and ultimately to the MBRF Trustees for review and funding consideration. The first Pilot Grant Program Awards were made in 2018 with the goal that these pilot research grant initiatives would position them for additional funding by the NIH or other sources.

Pilot Grant Awards:

A. June 1, 2018-- Vulnerability of Older Adults to Financial Deception Schemes—A Novel Intervention Tool--$60,000 per year for two years. The proposal will involve collaboration from investigators from three MBI sites and is designed to test intervention to reduce susceptibility to financial scams in older adults. Specifically, it is anchored in the important social and cognitive issues associated with age-related cognitive decline and memory loss. The proposed study would develop a prototype scam detection intervention software which would be used in the future to assist seniors in recognition and prevention from being scammed.

- Principal Investigators:
  Dr. Bonnie Levin, UM
  Dr. Sarah Getz, UM
  Dr. Robert Wilson and Dr. Matthew Grilli, UA
  Dr. Natalie Ebner and Dr. Daniella Oliveira, UF (Dr. Oliveira withdrew in July 2020)

B. June 1, 2018—A Pilot Intervention with Near Infrared Stimulation: Revitalizing Cognition in Older Adults. --$60,000 per year for two years. The study involves collaboration between investigators from two McKnight Brain Institute sites. The goal of the study is to evaluate the potential of near infrared non-invasive brain stimulation for remediating age-related cognitive decline. The study proposes a neuromodulation method that is highly novel based on the use of infrared light to impact underlying mitochondrial activity in the brain. The proposed mechanism of action differs from other non-invasive neuromodulation approaches that focus on neuroplasticity (e.g.), transcranial direct current stimulation).

- Principal Investigators:
  Dr. Dawn Bowers, UF
  Dr. Adam Woods, UF
  Dr. Gene Alexander, UA

C. July 31, 2019-- Transcutaneous Vagal Nerve Stimulation and Cognitive Training to Enhance Cognitive Performance in Healthy Older Adults--60,000 per year for two years., beginning October 1, 2019. The study is designed to evaluate the pairing of cognitive training and non-invasive neurostimulation technology that has shown promise in both increasing neuroplasticity and in enhancing cognitive performance through transcutaneous vagal nerve stimulation.

- Principal Investigators
  Dr. John B. Williamson, UF
  Dr. Gene Alexander, UA
  Dr. Ronald A. Cohen, UF
  Dr. Damon Lamb, UF
  Dr. Eric Porges, UF
  Dr. Adam Woods, UF

5. October 23, 2019—Evelyn F. McKnight Neurocognitive Post-Doctoral Fellowship Program for $200,000 ($100,000 per year for two years with starting date July 1, 2020) The MBRF Trustees approved the request from the Evelyn F. McKnight Brain Institute (MBI) at the University of Miami (UM) to support a fully funded two-year post-doctoral clinical fellowship dedicated to study age-related cognitive decline and memory loss. The MBRF Trustees approved funding as inaugural funding for the two-year clinical fellowship with the expectation that the MBI at the University of Miami would secure funding from other sources or provide the funding after 2022.

- Evelyn F. McKnight Neurocognitive Scholar:
  Christian Agudelo, M.D., was named the Evelyn F. McKnight Neurocognitive Scholar in March of 2020, starting his position in July 2020.

6. February 5, 2020—Supplemental Grant Award, Precision Aging Project, U-19 Proposal--$244,400. In 2019, Dr. Carol Barnes, director of the MBI at UA submitted a proposal to the National Institutes of Health for a U19 grant entitled **"Precision Aging Network: Closing the Cognitive Healthspan, Human Lifespan Gap".** The proposal was an enormous undertaking, with ~40 individuals

6. Continued…

participating. The proposal was reviewed by NIH, but Dr. Barnes, the PI of the U19 grant, and the associate directors of the grant, were notified additional intake information on the different demographic of participants (Spanish speaking cohort).in the study was required. The PI was also informed that application could be made for pilot support from his Strategic Initiative fund to mount a study to collect preliminary data for the U19 resubmission. The University of Arizona has contributed some matching funds to support the pilot project, but the supplemental pilot project was to be performed at the UM MBI for which there are no budget funds. Because of the importance and magnitude of the Precision Aging U-19 grant proposal and its potential contribution to the understanding and alleviation of age-related cognitive decline and memory loss, the Trustees approved the request for $244,400 to support the supplemental project to the Precision Aging U-19 Grant.

7. February 26, 2021--Harnessing Optimal Mechanisms of Exercise for Cognitive Gains (HOME-Cog) -- $60,000 per year beginning May 1, 2021. The current proposal outlines a collaborative project between the Evelyn F. McKnight Brain Institutes (MBI) at University of Miami and University of Florida that aims to inform the knowledge gap on the mechanistic action of exercise on the brain by characterizing important mechanisms of neuroplasticity and cardiovascular capacity, proposed to underlie cognitive response to exercise.

- Principal Investigators
  Joyce Gomes-Osman, PT, PhD, UM
  Katalina McInerney, PhD (Co-Investigator), University of Miami
  Mitchell Slugh, PhD, (Co-Investigator University of Miami
  Tatjana Rundek, MD, PhD (Co-Investigator), University of Miami
  Bonnie Levin, PhD (Co-Investigator), University of Miami
  David Loewenstein, PhD (Co-Investigator), UM
  Alvaro Pascual-Leone, MD, PhD (Co-Investigator), Professor of Neurology, Harvard Medical School
- Collaborators
  Eric Porges, PhD, UF
  Joseph Gullett, Research Assistant Professor, UF
  Adam Woods, PhD, UF
  Ronald Cohen, PhD, UF

8. February 26, 2021--Improving Age-Related Cognitive Decline with Exercise in Hypertensive Older Adults: A Pilot Study to Investigate a Retinal Microvascular Biomarker and the Role of IGF-1--$56,144 per year for two years. The study is designed to examine the relationship of retinal microvascular density, IGF-1 and cognitive function in older individuals with essential hypertension. The goal of the study is to determine whether an exercise intervention will improve age-related growth factor deficiencies and retinal microvascular density, and, in turn, be associated with an improvement in cognition

- Principal Investigator
  Ronald M. Lazar, PhD (UAB)
- Collaborators
  Christopher Girkin, MD, MSPH (UAB)
  Marcas Bamman, PhD (UAB)
  Tatjana Rundek, MD, PhD (UM)
  Jianhua Wang, MD, PhD (UM)

9. September 28, 2021—The Precision Aging Network: "**Closing the Cognitive Healthspan, Human Lifespan Gap"** grant submitted by Dr. Carol Barnes, Director of the Evelyn F. McKnight Brain Institute at the University of Arizona has been awarded a five-year $60 million grant from the National Institutes of Health to create and lead that could transform the way we think about the aging brain. Dr. Barnes will lead the network and bring together researchers from across the country to better understand how and why people experience brain aging differently, with the ultimate goal of developing more effective treatments and interventions targeted to the individual.

10. May 1, 2023 --"Feasibility of a Timed Bright Light Exposure Therapy to Improve Circadian Function". The purpose of the study is to examine the feasibility and tolerability of timed bright light exposure therapy to enhance circadian function in the oldest old. Award: $60,000 per year for two years.

- Principal Investigators
  Sonya Kaur, PhD
  Karem Gamble, PhD
- Mentors
  Bonnie Levin, PhD
  Alberto Ramos, PhD

11. May 1. 2023--Ketogenic Diet Improvement of Age-Related Memory Impairments, Nominates Cell-type Specific O-GicNAc Deficiencies in the Aged Hippocampus". The study is designed to investigate the contribution of metabolic O-linked N-acetylglucosamine (O-GlcNAc). The research is targeted toward gaining a greater understanding of the underlying metabolic mechanisms involved in the benefit of Ketogenic diet therapy on improvement of memory impairments associated with age. Award: 2 years. Year 1; $53,434; Year 2: $64,391.

- Principal Investigator
  Farah D. Lubin, PhD
- Co-Principal Investigator
  Matthew Huentelman, Ph.D.

12. May 1, 2023 -- "Cued High-Speed Multidirectional Yoga: Impact on Retinal Microvascular and Cognitive Measures". The proposed YogaCue program includes high-speed intervals to address cardiovascular fitness, and multi-directional responses to visual and auditory cuing, with pattern recognition and retention to address multiple cognitive domains. We will use changes in the retina microvasculature and capillary function and targeted cognitive testing to assess the success of the Yoga Cue program. Award: 2 years; Year 1: $59,997; Year 2: $59742

- Principal Investigator
  Joseph F. Signorile, PhD
- Co-Principal Investigators
  Jianhua Wang, MD, PhD
  Hong Jiang, MD, PhD
  Natalie Ebner, PhD,

McKnight Brain Research Foundation Inter-Institutional Meetings

- Annual meeting of all research scientists from each of the four McKnight Brain Institutes.
- Each McKnight Brain Institute rotates hosting each inter-institutional meeting.
- Annual cost supported by McKnight Brain Research Foundation
- Annual Budget: $100,000 plus Trustee travel and meeting expenses*
- 2008: 1st meeting hosted by Evelyn F. McKnight Brain Institute at the University of Arizona
- Cognitive Aging Summit III symbolizes the 10th anniversary of the Inter-institutional meetings
- 14th Inter-institutional meeting was held May 3-5, 2023, and was hosted by the Evelyn F. McKnight Brain Institute at the University of Alabama at Birmingham

* Because of inflationary pressure, the 2023 budget was approved not to exceed $130,000.

Prevention and Mitigation of Cognitive Decline: From the Bench to Community Engagement

May 3 - 5, 2023
Hilton at UAB, Birmingham, Alabama

Wednesday, May 3, 2023

12:00 – 5:00 PM	MBRF Board Meeting Montgomery Boardroom, Lower Level
1:00 – 6:00 PM	Registration Foyer - outside Hamilton II, Lower Level
5:30 – 7:30 PM	Opening Reception Collum Parlor and Pool Terrace, Lobby Level

6:00 PM **Welcome Remarks**

Ronald M. Lazar, PhD
Director, Evelyn F. McKnight Brain Institute
Evelyn F. McKnight Chair for Learning and Memory in Aging
Professor of Neurology & Neurobiology
University of Alabama at Birmingham

Anupam Argarwal, MD
Dean, Heersink School of Medicine
University of Alabama at Birmingham

Tom Brannan
Vice President for Advancement and Strategic Initiatives
University of Alabama at Birmingham

Michael L. Dockery, MD
Chair, McKnight Brain Research Foundation

Thursday, May 4, 2023

7:30 – 8:40 AM	General Breakfast Hamilton II, Lower Level

7:30 – 8:40 AM	Intervention Core Meeting Montgomery Boardroom, Lower Level
8:45 – 9:10 AM	**Opening Remarks and Welcome** Hamilton I, Lower Level Jason J. Nichols, OD, MPH, PhD Senior Associate Vice President for Research University of Alabama at Birmingham **Overview of Meeting Structure** Ronald M. Lazar, PhD Director, Evelyn F. McKnight Brain Institute University of Alabama at Birmingham Tatjana Rundek, MD, PhD Director, Evelyn F. McKnight Brain Institute University of Miami “Remembering Ralph Sacco”
9:10 – 9:45 AM	**Opening Lecture** Steven Austad, PhD Protective Life Endowed Chair in Health Aging Research Distinguished Professor University of Alabama at Birmingham “Translating the Biology of Aging into the Community”
9:45 – 9:55 AM	Discussion
9:55 – 10:15 AM	Break
10:15 – 11:30 AM	**MBAR Update** Moderator: Tatjana Rundek, MD, PhD
10:15 – 10:35 AM	Ron Cohen, PhD, ABPP University of Florida “Part 1: Where we came from and why?”
10:35 – 10:55 AM	Kristina Visscher, PhD University of Alabama at Birmingham “Part 2: Where we are, accomplishments, and successes”
10:55 – 11:15 AM	Bonnie Levin, PhD University of Miami “Part 3: Where are we going?”
11:15 – 11:30 AM	Discussion

11:30 – 12:20 PM	**Invited Speaker** Philip B. Gorelick, MD Professor of Neurology The Ken and Ruth Davee Department of Neurology Northwestern Feinberg School of Medicine “Optimizing Brain Health”
12:20 – 12:30 PM	Discussion
12:30 – 1:45 PM	Lunch and Networking Hamilton II, Lower Level
1:45 – 3:05 PM	**Implementing Successful Aging into the Community** Moderator: Carol Barnes, PhD
1:45 – 2:05 PM	Asta Håberg, MD, PhD Norwegian University of Science and Technology “Sociocultural Factors in the Longitudinal Study of Aging”
2:05 – 2:25 PM	Matt Huentelman, PhD University of Arizona MindCrowd
2:25 – 2:45 PM	Pamela Bowen, CRNP, PhD University of Alabama at Birmingham “Brain Health Advocacy Mission (BHAM)”
2:45 – 3:05 PM	Discussion
3:05 – 3:25 PM	Break
3:25 – 4:40 PM	**Workshop in Implementation Science** Moderator: Lee Ryan, PhD
3:25 – 3:45 PM	Heidi Hamann, PhD University of Arizona “Fundamentals of Implementation Science”
3:45 – 4:05 PM	George Howard, DrPH University of Alabama at Birmingham “Randomized Controlled Trials: What they are and are not”
4:05 – 4:25 PM	Fern Webb, PhD University of Florida “Conducting studies in diverse and underserved populations”
4:25 – 4:40 PM	Discussion

4:40 – 5:30 PM	Free time before Evening Event
5:30 – 6:00 PM	Transportation to The Florentine Ballroom (dress: business attire; distance is 1.0 mile away from Hilton at UAB)
6:00 – 9:00 PM	**Dinner and Guest Speaker** M. Joycelyn Elders, MD Vice Admiral 15th Surgeon General of the United States
5:45 – 6:45 PM	Reception
6:45 PM	Begin Seated Dinner
7:30 – 8:15 PM	Dr. Elders keynote presentation and Q&A
8:15 – 9:00 PM	Dessert and Social
8:45 – 9:15 PM	Transportation to Hilton at UAB

Friday, May 5, 2023

7:00 – 8:30 AM	Breakfast and Checkout (check-out time is 12pm) Hamilton II, Lower Level
7:30 – 8:30 AM	Board Meeting, Trustees and Leadership Council Skipwith I, Lower Level
8:15 – 8:30 AM	Load buses for departure to campus
8:45 AM	Buses depart for UAB National Alumni House Main Conference Room
9:15 – 10:10 AM	**Pre-Clinical Models for Intervention: Mechanisms and Outcomes** Moderator: Jennifer Bizon, PhD
9:15 – 9:30 AM	Stephen Cowen, PhD University of Arizona “The impact of aging on hippocampal representations of space and motion”
9:30 – 9:45 AM	Barry Setlow, PhD University of Florida “Differential effects of cannabis on cognition across the lifespan”

9:45 – 10:00 AM	Oliver Bracko, PhD University of Miami “Vascular oxidative stress causes neutrophil arrest in brain capillaries, leading to decreased cerebral blood flow and contributing to memory impairment”
10:00 – 10:10 AM	Discussion
10:10 – 11:00 AM	**Optical Coherence Tomographic Angiography: A Novel Biomarker for Aging** Moderator: Sara Burke, PhD
10:10 – 10:30 AM	Edmund Arthur, OD, PhD University of Alabama at Birmingham “Retinal Perivascular Spaces in Aging”
10:30 – 10:50 AM	Jinhua Wang, MD, PhD University of Miami “Current status and future direction of the eye as the window to the aging brain”
10:50 – 11:00 AM	Discussion
11:00 – 11:15 AM	**Closing Remarks** Ronald M. Lazar, PhD Director, Evelyn F. McKnight Brain Institute University of Alabama at Birmingham Molly V. Wagster, PhD Chief, Behavioral & Systems Neuroscience Branch Division of Neuroscience National Institute of Aging Michael L. Dockery, MD Chair, McKnight Brain Research Foundation
11:15 AM	Pick-up Boxed Lunches
11:30 AM	Buses depart for Hilton at UAB (1 or 2 buses will depart for Airport in afternoon, times tba)
1:00 PM – 4:30 PM	**Optional, Post-Meeting Event** (additional information, tba)
1:00 PM	Bus departs Hilton at UAB for Birmingham Civil Rights Institute (BCRI)

1:30 – 2:50 PM	Tour of the BCRI
3:00 – 4:00 PM	Tour of the 16th Street Baptist Church (distance is 0.1 mile away from BCRI, we will walk to)
4:00 PM	Bus departs for Hilton at UAB

The Precision Aging Network
September 28, 2021

The Precision Aging Network: "**Closing the Cognitive Healthspan, Human Lifespan Gap"** grant submitted by Dr. Carol Barnes, Director of the Evelyn F. McKnight Brain Institute at the University of Arizona has been awarded a five-year $60 million grant from the National Institutes of Health to create and lead that could transform the way we think about the aging brain. Dr. Barnes will lead the network and bring together researchers from across the country to better understand how and why people experience brain aging differently, with the ultimate goal of developing more effective treatments and interventions targeted to the individual.

Research Partnership in Cognitive Aging

2009—The Research Partnership in Cognitive Aging between the National Institute on Aging (NIA) and the McKnight Brain Research Foundation (MBRF) was established to support the funding of competitive grant research proposals in cognitive aging through the Foundation for the NIH (FNIH).

- Agreement by the MBRF and the NIA was reached for each organization to provide a minimum of $1 million each for a period of five years to fund proposals for research in cognitive aging and age-related memory loss to be vetted by the NIA process and procedures.
- For the first five-year cycle the MBRF contributed $5 million and the NIA and other partners contributed $23 million.
- Requests for applications targeted two research areas:

  1) Interventions to remediate age-related cognitive decline

  2) Neural and behavioral profiles of cognitive aging

- 17 five-year research proposals were funded

2014 – The Research Partnership in Cognitive Aging was renewed

- Funded a five-year clinical trial *"Cognitive Decline: Mindfulness-based Stress Reduction and Exercise"*
- MBRF's contribution was $5 million; NIA's contribution was $15 million

2019 – The Research Partnership in Cognitive Aging was renewed

- Funded a five-year concept for development *"Network for Identification, Evaluation and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age."*
- The funding opportunity announcement has been posted on Grants.NIH.Gov. Letters of Intent were due September 1, 2020, and applications due October 1, 2020, but were delayed until May 2021, but was delayed until May 2021.

- MBRF's contribution: $5 million. The unofficial contribution from the NIA is expected to be a three for one match for a total of $15 Million from the NIA. Both MBRF and NIA contributions are payable over five years).

Research Partnership in Cognitive Aging

A report to the McKnight Brain Research Foundation

January 12, 2023

Foundation for the National Institutes of Health
National Institute on Aging

Report Summary

Two initiatives currently form the centerpiece of a Research Partnership in Cognitive Aging between the McKnight Brain Research Foundation (MBRF) and the National Institute on Aging (NIA), coordinated by the Foundation for the National Institutes of Health (FNIH) – "Plasticity and Mechanisms of Cognitive Remediation in Older Adults" and "Network for Identification, Evaluation, and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age." One is drawing to a close now that the trial has ended and the results have been published. The other still is in the early stages and we look forward to continued progress over the next four years.

The FNIH is pleased to present this 2022 report to the MBRF. It provides updates from the NIA on the MEDEX trial and the Cognitive Superagers Networks, both supported through the Research Partnership in Cognitive Aging, as well updates on two additional initiatives that stemmed from the Cognitive Aging Summit III.

"Plasticity and Mechanisms of Cognitive Remediation in Older Adults (R01)"

Link to NIA Request for Applications: RFA-AG-14-016

Remediating Age-related Cognitive Decline: Mindfulness-based Stress Reduction and Exercise (MEDEX)

The MEDEX clinical trial (R01 AG049369), awarded to Eric Lenze, M.D. at Washington University in St. Louis, is complete and the results were published in *JAMA* in December 2022. Top line findings were that neither exercise nor mindfulness-based stress reduction, or the combination of the two, was better than placebo in impacting cognitive performance or brain structure in older adults. See Appendix A for the original abstract describing the plan for the MEDEX trial. The *JAMA* article describing the results is Appendix B. Washington University's press release about the results is at the following link: https://medicine.wustl.edu/news/exercise-mindfulness-dont-appear-to-boost-cognitive-function-in-older-adults/

Note:

The participants in the MEDEX trial will continue to be followed through a new award (R01AG072694, "Resilience and Brain Health of Older Adults During the COVID-19 Pandemic") to Dr. Lenze (Washington University St. Louis), Dr. Breno Diniz (University of Connecticut School of Medicine), and Dr. Julie Wetherell (University of California San Diego).

This project will elucidate whether exercise and mindfulness can mitigate the effects of pandemic stress on cognitive function and emotional health in later life, including neurobiological measures of risk for Alzheimer's Disease. The team will leverage the MEDEX trial. By doing so, and following the participants, who continue to attend monthly booster sessions of their randomized condition remotely during the pandemic, they will generate repeated sets of clinical, cognitive, molecular, and neuroimaging measures spanning 7.5 years and covering the pre-, during-, and post-pandemic period.

"Network for Identification, Evaluation, and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age (U19 Clinical Trial Not Allowed)"
Link to NIA Request for Applications: RFA-AG-21-015

Resilience/Resistance to Alzheimer's Disease in Centenarians and Offspring (RADCO)
U19AG073172
The RADCO cooperative agreement (U19AG073172), awarded to Drs. Thomas Perls (Boston University Medical Campus), Stacy Andersen (Boston University Medical Campus), and Susan Bookheimer (UCLA) is in the second year of award. The NIA is supporting a multi-year administrative supplement to enhance diversity and data capture. The supplement funds a fourth phenotyping and biospecimen core and neuroimaging core site at Georgia State University (GSU). Addition of the GSU site will enhance the diversity of the RADCO cohort by enrolling 234 African Americans, thus increasing the proportion of the RADCO sample that is African American from 7.2% to 22.2%.

The abstract for U19AG073172:

DESCRIPTION (provided by applicant): Centenarians delay age-related diseases and disabilities into their mid-nineties. Some remain cognitively intact despite extreme exposure to the strongest risk factor for cognitive impairment and AD, aging. The overall hypothesis of this study, titled "Resilience/Resistance to AD in Centenarians and Offspring" (RADCO), is: centenarian cognitive superagers and some of their offspring have protective factors that confer such resilience or in some cases, even resistance against cognitive decline and dementia. RADCO assembles an unprecedentedly large sample of prospectively studied centenarian cognitive superagers (n=495, essentially, centenarians with cognitive function that falls within the norms of septuagenarians) along with offspring (n=600) and offspring spouses (n=120), who, via RADCO cores, undergo careful, comprehensive and cutting edge neuropsychological, biomarker, neuroimaging and neuropathological phenotyping. These data are used by two projects with the overall scientific objective of gauging cognitive resilience in this sample, understanding the underlying protective biology and translating that into therapeutic targets. The Cognitive Resilience and Resistance Phenotypes Project (Project 1) gauges resilience by neuroimaging, plasma AD biomarkers risk and neuropathology and therefore generates a range of resilience endophenotypes. The Protective Factors and Mechanisms Project (Project 2) is the translation arm of RADCO; it discovers genes, candidate biological pathways and sets of mi-RNA regulators associated with the resilience endophenotypes characterized in Project 1. In-vitro models of AD incorporate cortical neurons, microglial cells and astrocytes created from centenarian cognitive superager induced pluripotent stem cell (iPSC) lines are used to test the candidate pathways for how they cause resilience against AD.

PUBLIC HEALTH RELEVANCE: Centenarian cognitive superagers have exceptional cognitive function despite extreme exposure to the strongest risk factor for cognitive impairment and Alzheimer's disease, aging. The "Resilience/Resistance to AD in Centenarians and Offspring" (RADCO) Study gauges cognitive resilience among centenarian cognitive superagers and their offspring using cognitive testing, neuroimaging, blood biomarkers, and neuropathology and translational studies will identify protective factors and underlying mechanisms that confer resilience or in some cases, even resistance against cognitive decline and dementia.

Study to Uncover Pathways to Exceptional Cognitive Resilience in Aging (SUPERAging)
U19AG073153
The SUPERAging cooperative agreement (U19AG073153) awarded to Drs. Emily Rogalski, Marsel Mesulam, and Changiz Geula (Northwestern University of Chicago) is in its second year of award. The team published

findings in *Journal of Neuroscience* (see Appendix C) in late 2022 regarding brain structural differences in cognitive SuperAgers vs cognitively normal older adults. They reported that the size of neurons in the entorhinal cortex (ERC) of cognitive SuperAgers is significantly larger than ERC neurons in adults with amnestic mild cognitive impairment, than those of age peers with normal cognition for their age, than those of adults in their 50s and 60s. The authors suggest that larger ERC neurons are a biological signature of the cognitive SuperAging trajectory.

The abstract for U19AG073153:

DESCRIPTION (provided by applicant): The primary goal is to establish a multicenter SuperAging Consortium to identify behavioral, health, biologic, genetic, environmental, socioeconomic, psychosocial, anatomic and neuropathologic factors associated with SuperAging. These goals will be achieved through an organizational structure with 3 Cores (Administrative/Biostatistics, Clinical/Imaging, and Biospecimen/Neuropathology) and 2 Research Projects. The Consortium will enroll 500 participants across 4 US Sites located in Illinois, Wisconsin, Michigan and Georgia, and the Canadian Site in Southwest, Ontario, with a focus on the enrollment of Black SuperAgers and Cognitively Average Elderly Controls with similar demographics (Controls). The Administrative/Biostatistics Core will provide governance and fiscal oversight, maintain scientific integrity, and create a centralized biostatistics and database infrastructure to harmonize the goals and activities of the Cores, Sites, and Projects, with each other, with the NIA and with extramural collaborators. The Clinical/Imaging Core will standardize criteria for the uniform cross-site and multidisciplinary characterization of SuperAgers, streamline recruitment including that of Black participants, enter relevant information in the comprehensive database, support co-enrollment into Project 1, and encourage collaborative ventures aiming to understand the factors that promote SuperAging. The Biospecimen/Neuropathology Core will collect and bank brain tissue and blood products from SuperAging and Control cases, according to optimized procedures. It will render pathological diagnoses, quantitate selected markers of neurodegeneration and neuronal structure, coordinate the analyses of plasma biomarkers for Alzheimer's disease, and make specimens available for collaborative investigations. Project 1 will use state-of- the-art wearable technology to obtain real-time measurements in the course of everyday life to characterize quantitative parameters related to sleep, physical activity, autonomic responsivity, and social engagement to determine whether SuperAgers have relatively preserved and quantitatively determined physiologic and behavioral `complexity' compared to Controls. Project 2 will use transcriptomic, genetic, and protein profiling approaches to test the hypothesis that SuperAgers will demonstrate significant molecular differences in their central and peripheral immune and inflammatory system parameters compared to matched Control and Alzheimer's disease participants. By identifying neurobiologic features that contribute to superior memory performance in old age, outcomes from this Consortium will help isolate factors that promote successful cognitive aging and perhaps also prevent age-related brain diseases such as Alzheimer's disease.

PUBLIC HEALTH RELEVANCE: The proposed Consortium offers optimal organization for the accelerated recruitment of a racially diverse cohort of SuperAgers so that they can be more fully characterized neuropsychologically, neuropathologically, psychophysiologically, and molecularly. The planned activities of the Consortium will help isolate factors important for promoting successful cognitive aging and potentially also for avoiding age-related brain diseases such as Alzheimer's disease.

Additional Initiatives Stemming from the Cognitive Aging Summit III

Besides RFA-AG-21-015 that provided support for the two network grants to identify, evaluate and track cognitive superagers and which was jointly sponsored by the MBRF and the NIA, the NIA launched two additional research initiatives based on knowledge gaps and research opportunities identified from the Cognitive Aging Summit III:

One of the recommendations from the 2017 Summit was to support a longitudinal study of rats that would closely track the animals throughout their lives. That recommendation is now an action. NIA's Intramural Research Program (IRP) has a longitudinal study underway - STARRRS— Successful Trajectories of Aging: Reserve and Resilience in RatS. The award was made to Dr. Peter Rapp in the IRP. The study is on track to generate state-of-the-art neuroimaging, along with phenotypic results, non-invasive biological samples plus other indicators that NIA hopes will yield insight into the mechanisms of healthy neurocognitive aging. STARRS will create open- source data and a sample hub to be shared with the entire aging science community. The goal is to bring us closer to an understanding of the factors that contribute to successful versus unsuccessful neurocognitive aging. The first cohort of animals entered the study during the past year and data collection is underway.

Another recommendation from the 2017 Summit was to develop operational definitions of constructs such as cognitive reserve, resilience, compensation, etc. that could be used uniformly by researchers. The Summit brought together a multidisciplinary group of investigators with shared interest in research on age-related cognitive decline as well as cognitive reserve and resilience. There was unanimous agreement that a significant barrier to progress in the field was the lack of clear and universally accepted definitions of important concepts related to cognitive reserve and resilience and that it was imperative to address this deficit. An RFA (RFA-AG-18-024) was released by NIA, and one award was made to Dr. Yaakov Stern and Columbia University Health Sciences for a network grant titled "Collaboratory on Research Definitions for Cognitive Reserve and Resilience" (R24 AG061421).

Dr. Stern, and his co-investigators (Drs. Marilyn Albert, Carol Barnes, Roberto Cabeza, Alvaro Pascual-Leone, Peter Rapp), have completed the goals of the project. The website for the effort https://reserveandresilience.com/ contains information for three workshops that have been held to date, the latest being in late October 2021. The framework for operational definitions of reserve and resilience concepts are in press in *Neurobiology of Aging*, along with a Commentary by Dr. Wagster and Dr. King. Both should be published online shortly and will be made available to the Board within the next month.

The abstract for R24AG061421:

DESCRIPTION (provided by applicant): Research indicates that specific life exposures and genetic factors contribute to some people being more resilient than others, with lower rates of cognitive decline with aging, and reduced risk of developing Alzheimer's disease and related dementias (ADRD). There are likely several complex and highly interactive mechanisms that lead to these individual differences in vulnerability to decline, probably reliant on both structural and functional brain mechanisms. Key concepts often used in research in this area are cognitive reserve, brain reserve and brain maintenance. However, the definitions of these concepts differ across researchers, and the

translation from human to animal research is not well developed. Also, their relationship to other invoked concepts such as efficiency, capacity, and compensation are not well explicated. The goal of this project is to work towards achieving state-of-the-art definitions for these concepts to allow researchers to use common nomenclature. In addition, the goal is to validate approaches to help advance research on these approaches that will lead to better maintenance of brain and cognitive health and treatment and/or prevention of ADRD. To that end we will hold three cross-discipline workshops that will bring together investigators to discuss and come to consensus on these concepts, create focused workgroups that will examine each of these issues, fund pilot grants designed to further the understanding and research applicability of these concepts, and to develop data sharing and information exchange platforms to help guide promote research in this area.

PUBLIC HEALTH RELEVANCE: In order to achieve state-of-the-art definitions and research guidelines for key concepts associated with resilience against cognitive aging and Alzheimer's disease related dementia, this project will hold three multidisciplinary workshops, establish focused work groups, create a data sharing and information platform, and support pilot grants designed to further the understanding of these concepts.

Appendix A

MEDEX Trial Abstract (NIH Award R01AG049369):

DESCRIPTION (provided by applicant): The vast majority of older adults will suffer declines in cognitive functions such as memory and cognitive control (or executive function), interfering with their ability to participate and engage in meaningful activities. Importantly, the recent observation that the brain retains plasticity late into life suggests that timely and personalized interventions might remediate age- related cognitive decline. Two promising interventions are Mindfulness-Based Stress Reduction and Exercise, each of which appears to act in multi-modal ways to make plastic changes in CNS function to improve memory and cognitive control in older adults. Our research team has conducted several studies of these interventions, supporting their benefits and pathways to improved cognitive functioning. We propose a 2x2 factorial design RCT to definitively test MBSR and exercise for remediation of age-related cognitive decline. We will randomize 580 healthy community-living adults aged 65+ to one of four conditions: MBSR alone, exercise alone, MBSR + exercise, or health education (a control condition).
Participants will receive protocolized interventions for a six-month acute period, followed by a 12- month maintenance period. We will examine (1) cognitive improvements using a well-validated and sensitive neuropsychological battery focusing on memory and cognitive control; (2) mechanistic changes such as reduced cortisol and improved insulin sensitivity (3) neuroimaging markers of plasticity: structural and functional connectivity changes indicating plastic CNS changes underlying the cognitive improvements (4) individual variability that predicts response to the interventions. Our main goal is to carry out a high-quality clinical trial, such that data and biosamples will become a resource for the scientific community. Then, we can not only improve the lives of older adults in the near-term by matching individuals to readily available interventions that most benefit them, we can also understand the mechanisms of neuroplastic changes with interventions to rescue cognitive decline with aging, leading to a more active and vital senior community.

PUBLIC HEALTH RELEVANCE: The world is graying, and the vast majority of older adults will have declines in cognitive function, interfering with function, quality of life, and engagement in valued activities. We will test two promising interventions - Mindfulness Based Stress Reduction (MBSR) and Exercise - for their ability to remediate age-related cognitive decline. MBSR and exercise are both inexpensive, well-tolerated, safe, and highly scalable interventions; therefore, our project can demonstrate how effective they are, for whom, and by what mechanisms, in the near-term older adults could receive lifestyle strategies that would benefit their brain and cognitive functioning, staving off disability and dependence on others and maintaining engagement in life's most valued activities.

JAMA | Original Investigation

Effects of Mindfulness Training and Exercise on Cognitive Function in Older Adults
A Randomized Clinical Trial

Eric J. Lenze, MD; Michelle Voegtle; J. Philip Miller, AB; Beau M. Ances, MD; David A. Balota, PhD; Deanna Barch, PhD; Colin A. Depp, PhD; Breno Satler Diniz, MD, PhD; Lisa T. Eyler, PhD; Erin R. Foster, PhD; Torie R. Gettinger, PhD; Denise Head, PhD; Tamara Hershey, PhD; Samuel Klein, MD; Jeanne F. Nichols, PhD; Ginger E. Nicol, MD; Tomoyuki Nishino, MS; Bruce W. Patterson, PhD; Thomas L. Rodebaugh, PhD; Julie Schweiger; Joshua S. Shimony, MD; David R. Sinacore, PhD; Abraham Z. Snyder, MD; Susan Tate, PhD; Elizabeth W. Twamley, PhD; David Wing, MS; Gregory F. Wu, MD; Lei Yang, MPH, MSIS; Michael D. Yingling, MS; Julie Loebach Wetherell, PhD

IMPORTANCE Episodic memory and executive function are essential aspects of cognitive functioning that decline with aging. This decline may be ameliorable with lifestyle interventions.

OBJECTIVE To determine whether mindfulness-based stress reduction (MBSR), exercise, or a combination of both improve cognitive function in older adults.

DESIGN, SETTING, AND PARTICIPANTS This 2 × 2 factorial randomized clinical trial was conducted at 2 US sites (Washington University in St Louis and University of California, San Diego). A total of 585 older adults (aged 65-84 y) with subjective cognitive concerns, but not dementia, were randomized (enrollment from November 19, 2015, to January 23, 2019; final follow-up on March 16, 2020).

INTERVENTIONS Participants were randomized to undergo the following interventions: MBSR with a target of 60 minutes daily of meditation (n = 150); exercise with aerobic, strength, and functional components with a target of at least 300 minutes weekly (n = 138); combined MBSR and exercise (n = 144); or a health education control group (n = 153). Interventions lasted 18 months and consisted of group-based classes and home practice.

MAIN OUTCOMES AND MEASURES The 2 primary outcomes were composites of episodic memory and executive function (standardized to a mean [SD] of 0 [1]; higher composite scores indicate better cognitive performance) from neuropsychological testing; the primary end point was 6 months and the secondary end point was 18 months. There were 5 reported secondary outcomes: hippocampal volume and dorsolateral prefrontal cortex thickness and surface area from structural magnetic resonance imaging and functional cognitive capacity and self-reported cognitive concerns.

RESULTS Among 585 randomized participants (mean age, 71.5 years; 424 [72.5%] women), 568 (97.1%) completed 6 months in the trial and 475 (81.2%) completed 18 months. At 6 months, there was no significant effect of mindfulness training or exercise on episodic memory (MBSR vs no MBSR: 0.44 vs 0.48; mean difference, –0.04 points [95% CI, –0.15 to 0.07]; $P = .50$; exercise vs no exercise: 0.49 vs 0.42; difference, 0.07 [95% CI, –0.04 to 0.17]; $P = .23$) or executive function (MBSR vs no MBSR: 0.39 vs 0.31; mean difference, 0.08 points [95% CI, –0.02 to 0.19]; $P = .12$; exercise vs no exercise: 0.39 vs 0.32; difference, 0.07 [95% CI, –0.03 to 0.18]; $P = .17$) and there were no intervention effects at the secondary end point of 18 months. There was no significant interaction between mindfulness training and exercise ($P = .93$ for memory and $P = .29$ for executive function) at 6 months. Of the 5 prespecified secondary outcomes, none showed a significant improvement with either intervention compared with those not receiving the intervention.

CONCLUSIONS AND RELEVANCE Among older adults with subjective cognitive concerns, mindfulness training, exercise, or both did not result in significant differences in improvement in episodic memory or executive function at 6 months. The findings do not support the use of these interventions for improving cognition in older adults with subjective cognitive concerns.

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Visual Abstract

Supplemental content

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Most older adults experience deteriorating cognitive function. Declines in episodic memory and executive function parallel volume losses in brain structures, such as the hippocampus and dorsolateral prefrontal cortex (DLPFC).[1,2] With the increasing age of the population, lifestyle interventions could provide a scalable means to target modifiable mechanisms of these cognitive and brain changes, thereby helping improve and maintain cognitive functioning.[3]

Two promising interventions are mindfulness training and exercise. Mindfulness-based stress reduction (MBSR) is a group-based intervention based on mindfulness meditation training.[4] From a mechanistic standpoint, practicing mindfulness may enhance cognitive processes such as working memory[5]; further, mindfulness techniques may reduce stress, thereby affecting physiological parameters such as cortisol levels and sleep.[6,7] Aerobic and strength training are both theorized to be associated with cognitive function[8]; some studies have found exercise-related cognitive changes together with structural brain changes.[9,10] Previous studies have suggested changes in insulin sensitivity, aerobic capacity, and body fat as some of the proposed mechanisms.[11] MBSR and exercise could have additive benefits because their putative mechanisms may be complementary. Accordingly, a randomized clinical trial was conducted to determine whether MBSR and exercise improve cognitive function and whether the combination of MBSR and exercise has greater benefits than either intervention alone.

Key Points

Question Does mindfulness training, exercise, or the combination of these interventions improve cognitive function in older adults with subjective cognitive concerns?

Findings In this randomized clinical trial that included 585 participants, mindfulness training, exercise, or both did not result in significant differences in improvement in episodic memory or executive function composite scores at 6 months.

Meaning The findings do not support the use of mindfulness training, exercise, or a combination of both for significantly improving cognitive function in older adults with subjective cognitive concerns.

Methods

Study Design

The MEDEX (Mindfulness, Education, and Exercise) study was a randomized clinical trial comparing MBSR and exercise, alone or in combination, with a robust control intervention (health education) designed to control for expectancy in older adults with subjective cognitive concerns and without dementia. Outcome assessments evaluated cognitive function and brain structure over 18 months of intervention. For full details of the trial design, protocol, and statistical analysis plan, see Wetherell et al[12] and Supplement 1. The study was conducted from 2015 to 2020 in St Louis, Missouri, and San Diego, California, with enrollment from November 19, 2015, through January 23, 2019, and final follow-up on March 16, 2020. Ethics approval was provided by the universities' institutional review boards. All participants provided written informed consent. Recruitment methods included use of press (eg, television, newspapers), online sources (eg, via social media, websites), printed flyers, presentations at community outreach events, and direct mailings.

Participants

From November 2015 to January 2019, the study enrolled community-dwelling older adults. Inclusion criteria were age 65 to 84 years; self-reported age-related changes in cognitive function, defined by a positive response to questions of whether they or others had noticed trouble with their memory or concentration; and being cognitively intact, defined as scoring less than 10 on the Short Blessed Test, for which scores greater than or equal to 10 suggest impairment consistent with dementia.[13] The study allowed mild cognitive impairment, and no clinical rating of dementia status was done. Exclusion criteria were neurodegenerative illness (eg, dementia, Parkinson disease, cerebrovascular disease); not sedentary (current moderate- to high-intensity exercise ≥1 h/wk or light activity ≥1 h/d; see eMethods 1 in Supplement 2 for details); current meditation practice or cognitive training; medical conditions that suggest shortened lifespan, or would prohibit safe participation, would prohibit safe participation in the interventions (eg, metastatic cancer, unstable cardiovascular disease), or would interfere with study assessments (eg, diabetes medication, systemic glucocorticoids, magnetic resonance imaging [MRI] contraindications, severe hearing/visual impairment); and nonfluent English-language speaker.

Randomization

After baseline assessment, participants were randomized to the following groups in a 1:1:1:1 ratio: MBSR alone, exercise alone, combined MBSR and exercise, and health education (control group). Using R software, the study statistician (M.D.Y.) generated the randomization sequence. The study primary investigator and coordinators were kept blinded to the randomization until the study coordinator was ready for the next group to be randomized. Participants learned their randomization assignment at the first intervention group meeting. Randomization was done in groups of approximately 15 individuals (range, 12-17) and was stratified by site.

Interventions

All interventions were conducted for 18 months, which consisted of a 6-month acute and 12-month maintenance phase.

The MBSR intervention matched the format of the consensus MBSR protocol[14]; after a brief introductory meeting, the intervention was conducted in 8 weekly 2.5-hour classes plus a half-day retreat. For the remainder of the 6-month acute phase and the subsequent 12 months of maintenance, MBSR classes met monthly. Content included instruction in mindfulness meditation practices and exercises to enhance mindfulness in everyday life. Participants also used *A Mindfulness-Based Stress Reduction Workbook*.[15] Participants received daily

at-home assignments with a goal of 60 minutes of daily at-home meditative practice. Additional details are provided in Supplement 2.

The exercise intervention was designed to improve aerobic fitness, strength, balance, mobility, and flexibility. It consisted of facility-based, instructor-supervised 1.5-hour classes twice weekly for 6 months. Sessions included aerobic exercise, resistance training, and functional exercises. Participants were prescribed home exercise with a goal of completing at least 300 minutes per week of combined class plus home exercise. Classes continued once per week during the 12-month maintenance phase with the same exercise goal of at least 300 minutes per week. Additional details are provided in Supplement 2.

Participants in the combined MBSR and exercise intervention underwent both MBSR and exercise, with the above-listed frequency of classes and goals for each intervention.

The health education intervention was an attention placebo to control for nonspecific factors (eg, time spent in groups) and expectancy.[16] It matched the MBSR intervention for group setting, class time, frequency of sessions, and attention with weekly assignments, but no goals, related to the amount of time engaged in them. It was based on the Stanford chronic disease self-management book *Living a Healthy Life with Chronic Conditions*,[17] omitting information on mindfulness and exercise.

To monitor fidelity, both sites utilized instructors trained in the respective interventions. Instructor fidelity was maintained by regular supervision calls, measuring session time and confirming adherence to the study protocol, and, in the case of MBSR, video recording sessions with review by MBSR experts according to published fidelity criteria for mindfulness-based interventions[18] (all sessions were rated as competent; Supplement 2).

To evaluate participant adherence, class attendance was monitored. Additionally, for MBSR and exercise interventions, home practice during the 6-month acute period was measured and reinforced using daily surveys sent to tablets or smartphones. During the maintenance phase, participants in the MBSR and exercise groups were asked if they had any breaks in their home practice.

Outcomes

All outcomes were measured by blinded assessors. The 2 primary outcomes were episodic memory and executive function (cognitive control) composites (standardized to a mean [SD] of 0 [1]; higher composite scores indicate better cognitive performance) at the 6-month end point. These composite scores were calculated from a neuropsychological test battery conducted at 0, 3, 6, and 18 months. The secondary end point was 18 months. These domains were selected based on previous research on the effects of mindfulness and exercise on cognitive function. Memory tests were immediate and delayed recall using a 16-item word list and 2 paragraphs developed for repeated administrations during longitudinal studies (ie, different lists and paragraphs at each time point)[19] and the Picture Sequence Memory Test from the National Institutes of Health (NIH) Toolbox.[20] Executive function tests were the Dimensional Change Card Sort test, Flanker Inhibitory Control and Attention Test, and List Sorting Working Memory Test from NIH Toolbox and the following 3 additional computer-based tests: the Consonant-Vowel Odd-Even Switching test,[21] the Sustained Attention to Response Test,[22] and the Stroop Test.[23] For each memory or executive function variable, a Z score was computed for each participant using the mean and SD of that variable computed on all randomized participants at baseline ([participant score − mean]/SD). Composite scores were then created by taking the mean of the Z scores of all available memory or cognitive control variables (additional details are provided in the statistical analysis plan [Supplement 1]). Composite scores, compared with individual test scores, improve both test-retest reliability and the ability to detect subtle changes in scores, as exemplified by the Preclinical Alzheimer Cognitive Composite (a clinical trial outcome that similarly combines multiple cognitive tests).[24] For interpretation purposes, if the intervention was effective in improving each individual measure that comprised the composite by 1 SD, the overall composite score would improve by 1 point (compared with the control). The correlations between the baseline (month 0) and 6-month composite scores were 0.81 for the memory composite and 0.80 for the executive function composite, suggesting high reliability.

Secondary outcomes (left and right hippocampal volume and left and right DLPFC surface area and cortical thickness) consisted of high-resolution T1-weighted MRI (MP-RAGE; 1 × 1 × 1 mm; TR = 2300 ms; TI = 900 ms; TE = 2.95 ms; flip angle = 9°), which were acquired at 0, 6, and 18 months. Longitudinal FreeSurfer[25] processing generated the measurements. The correlations between the baseline and 6-month MRI measures were 0.99 for hippocampal volume, 0.98 for DLPFC surface area, and 0.92 for DLPFC thickness. At the same time points, resting-state MRI data were collected; these data are presented in another report.[26]

Additional secondary cognitive outcomes included the Revised Observed Tasks of Daily Living[27] score, a performance-based measure of functional cognitive capacity (range, 0-28; higher values indicate greater ability to complete everyday activities) and the Quality of Life in Neurological Disorders Cognitive Function[28] score, a self-report measure of cognitive concerns (range, 18-90; higher values indicate better outcomes).

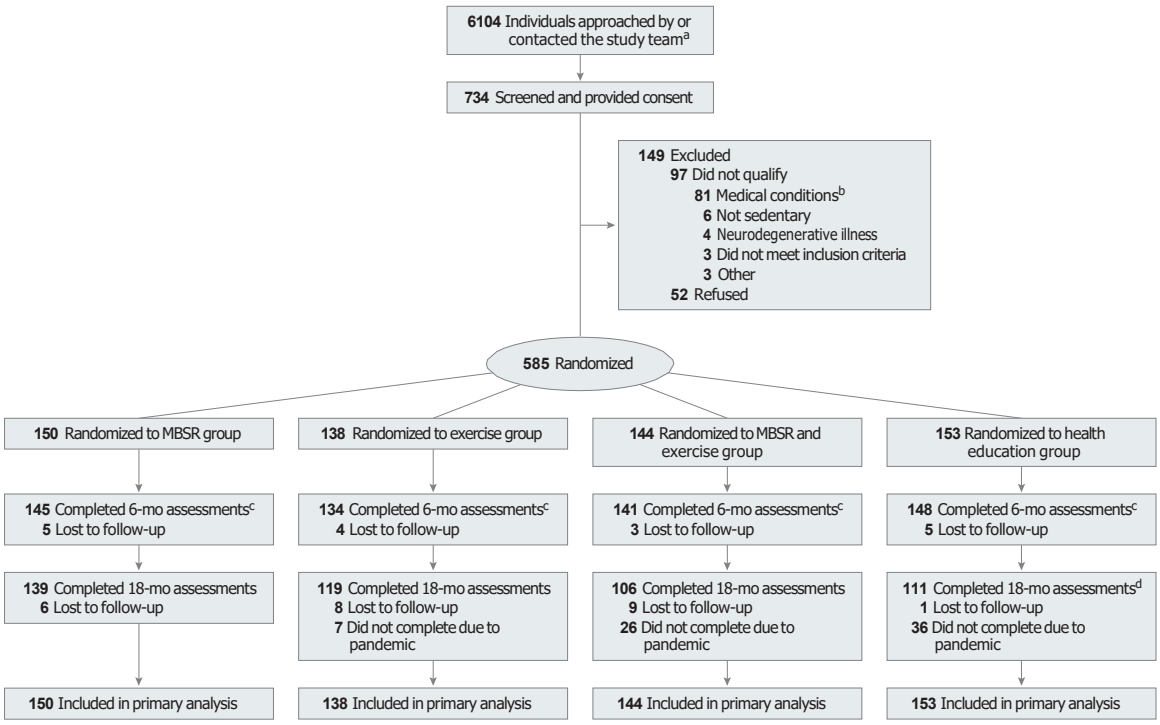
To assess mechanisms of exercise- and mindfulness-induced cognitive benefits, several physiological and performance measures at 0, 6, and 18 months were tested (details of measurement are provided in Supplement 2): aerobic fitness, insulin sensitivity and resistance, body fat and fat-free masses, physical performance, plasma cortisol levels, physical activity, time to fall asleep and total sleep time, mindfulness state, and upper- and lower-body strength.

Race and ethnicity were self-reported by participants based on fixed categories to understand the diversity of enrolled participants and for potential future subgroup analyses examining differences in results based on these characteristics.

Sample Size Calculation

A target sample size of 580 participants was determined based on 80% power to detect either main effects or an interaction of

Figure 1. Participant Flow in a Study of the Effect of Mindfulness-Based Stress Reduction (MBSR) and Exercise on Cognitive Function



[a] Unless individuals were screened, they were not fully assessed for eligibility; as such, the study team does not have the results (eg, why they were excluded or declined) for all of these individuals.

[b] Conditions that would suggest shortened lifespan or would prohibit safe participation in the interventions (eg, metastatic cancer, unstable cardiovascular disease) or would interfere with study assessments (eg, diabetes medication, systemic glucocorticoids, magnetic resonance imaging contraindications, severe hearing/visual impairment).

[c] Unless they officially withdrew, participants who missed the 6-month assessment were not out of the study; they could rejoin for the 18-month assessment.

[d] A higher number of participants (n = 36) in the health education intervention group were unable to complete the 18-month assessments due to the COVID-19 pandemic because of the randomization schedule (eg, these intervention groups were the last groups to be randomized in the trial). For example, 3 of the last 4 groups randomized in the trial were health education.

at least a small effect size, of 0.2 (Cohen *d*). The study was not designed to detect a specific minimal clinically important difference. All power analyses were conducted with G*Power, version 3.1, and assumed 15% attrition for power calculations.

Statistical Analyses

See Supplement 1 for the complete statistical analysis plan. A marginal model was fit for the repeated measures analyses. The model included the between-participant main effects of MBSR and exercise, their interaction, and the 2- and 3-way interactions between time and the between-participant effects. Time (0, 3 [cognitive measures only], 6, and 18 months) was a within-participants effect with an unspecified covariance matrix due to uneven time intervals between visits. Site, age, and sex were included as covariates in the models. Clustering by site was accounted for because site was a factor in all primary and secondary outcome models.

The primary test of effectiveness of each intervention was the change in the composite scores from baseline to 6 months in the participants randomized to undergo the intervention compared with those not receiving the intervention, as computed with the appropriate contrast (eg, MBSR vs no MBSR). The 2 × 2 factorial design was analyzed with the 2 main effects of exercise (underwent exercise intervention vs did not undergo exercise) and MBSR (underwent MBSR intervention vs did not undergo MBSR).

All randomized individuals were included in the primary analysis (Figure 1). Participants were analyzed according to their randomization group. A Bonferroni-adjusted 2-tailed significance level of .025 was used for each of the 2 primary outcomes. Effect sizes with 95% CIs for 6- and 18-month effects for all primary and secondary outcomes were computed. Because of the potential for type I error due to multiple comparisons, findings for analyses of secondary time points and secondary outcomes should be interpreted as exploratory. The mixed-model analytic approach used is robust in accounting for missing data. Participants were included in the analytic model if they had data for at least 1 time point.

Given neutral findings for the primary outcomes, the importance of post hoc analyses became clear. Subsequent per-protocol analyses were conducted, as were subgroup tests examining changes in cognitive outcomes among those who

showed the most vs the least change in the physiological and performance markers described above. The 2 per-protocol groups were defined post hoc based on examination of attendance data and home practice data: participants reporting home practice of their randomized intervention (MBSR or exercise) on at least 70% of days and participants attending at least 70% of classes. Both groups also excluded individuals who participated in interventions to which they were not randomized (Supplement 2). Additionally, given that the primary outcomes showed no intervention effect, the original plan to examine MRI structural changes as part of a mediator analysis was modified: rather than examining MRI structural changes as mediators, they were analyzed as secondary outcomes. All analyses were conducted in SAS, version 9.4 (SAS Institute).

Results

Enrollment and Participant Characteristics

A total of 6104 individuals were approached by or directly contacted the study team and 734 completed baseline screening and provided written informed consent; of these individuals, 149 did not qualify or wish to participate further. Thus, 585 individuals met all study criteria and were randomized and included in the analysis. A total of 97.1% of participants completed 6-month assessments and 81.2% completed 18-month assessments (Figure 1).

The full sample had a mean (SD) age of 71.5 (4.8) years and education level of 16.2 (2.2) years and 424 (72.5%) were women, 2 (0.3%) were American Indian, 27 (4.6%) were Asian, 69 (11.8%) were Black, 477 (81.5%) were White (the remaining individuals were unknown or >1 race), and 39 (6.7%) were Hispanic/Latino. Demographic information and other baseline characteristics were well-balanced across intervention groups (Table).

Primary Outcomes

Figure 2 shows changes over 18 months in the 2 primary outcome measures: composite variables of memory and executive function. At 6 months, there were no significant differences in these measures when comparing participants with and without MBSR (memory composite score, 0.44 vs 0.48; mean difference, –0.04 points [95% CI, –0.15 to 0.07]; $P = .50$; executive function score, 0.39 vs 0.31; mean composite difference, 0.08 [95% CI, –0.02 to 0.19]; $P = .12$) and with vs without exercise (memory composite, 0.49 vs 0.42; mean difference, 0.07 points [95% CI, –0.04 to 0.17]; $P = .23$; executive function composite, 0.39 vs 0.32; mean difference, 0.07 points [95% CI, –0.03 to 0.18]; $P = .17$).

Secondary Outcomes

There were also no significant differences at 18 months (secondary end point) for the composite variables of memory (MBSR vs no MBSR: 0.61 vs 0.53; mean difference, 0.08 [95% CI, –0.04 to 0.19]; $P = .18$; exercise vs no exercise: 0.55 vs 0.59; mean difference, –0.04 [95% CI, –0.15 to 0.07]; $P = .47$) and executive function (MBSR vs no MBSR: 0.27 vs 0.31; mean difference, –0.04 [95% CI, –0.15 to 0.07]; $P = .44$; exercise vs no exercise: 0.28 vs 0.29; mean difference, –0.01 [95% CI, –0.12 to 0.11]; $P = .93$)

Secondary outcomes included structural MRI measures (Figure 3) and additional cognitive outcomes (Supplement 2). At 6 months, there were no significant intervention effects on hippocampal volume (MBSR vs no MBSR: difference, –3.46 mm^3 [95% CI, –14.27 to 7.34]; $P = .53$; exercise vs no exercise: difference, 3.04 mm^3 [95% CI, –7.76 to 13.85]; $P = .58$), DLPFC surface area (MBSR vs no MBSR: difference, 22.71 mm^2 [95% CI, –22.95 to 68.36]; $P = .33$; exercise vs no exercise: difference, –17.18 mm^2 [95% CI, –62.83 to 28.48]; $P = .46$), or cortical thickness (MBSR vs no MBSR: difference, –0.01 mm [95% CI, –0.02 to 0.01]; $P = .37$; exercise vs no exercise: difference, 0.01 mm [95% CI, 0.00-0.02]; $P = .21$). At the secondary time point of 18 months, there was also no significant intervention effects on DLPFC surface area (MBSR vs no MBSR: difference, 25.35 mm^2 [95% CI, –23.18 to 73.88]; $P = .31$; exercise vs no exercise: difference, 21.11 mm^2 [95% CI, –27.41 to 69.64]; $P = .39$) or cortical thickness (MBSR vs no MBSR: difference = –0.01 mm, [95% CI, –0.02 to 0.00], $P = .10$; exercise vs no exercise: difference, –0.01 mm [95% CI, –0.02 to 0.00]; $P = .09$). One exception was that hippocampal volume showed a significantly greater reduction over 18 months with MBSR compared with no MBSR (difference, –20.16 mm^3 [95% CI, –33.88 to –6.44]; $P = .004$), contrary to the hypothesized direction of change; however, there was no significant intervention effect with exercise compared with no exercise (difference, –6.26 mm^3 [95% CI, –19.98 to 7.46]; $P = .37$). There was also a main effect of time for hippocampal volume ($P < .001$) and DLPFC cortical thickness ($P < .001$) (but not DLPFC surface area [$P = .68$]), which declined in all groups over 18 months. There were no significant intervention effects on the secondary cognitive outcomes (Observed Tasks of Daily Living or Neurological Disorders Cognitive Function score; eFigure 2 in Supplement 2).

Tests of Combination MBSR and Exercise and Intervention Interactions

Interactions between the 2 factors in the 2 × 2 design (MBSR vs no MBSR and exercise vs no exercise) were tested. Because none of the interaction test results were significant at 6 months (memory composite, $P = .93$; executive function composite, $P = .29$; hippocampal volume, $P = .76$; DLPFC surface area, $P = .19$; and DLPFC cortical thickness, $P = .52$), the primary analyses described above were conducted by pooling the factorial groups. eTable 1 in Supplement 2 presents a 4-group analysis (MBSR alone, exercise alone, combined MBSR and exercise, and health education), along with full data on the 3-way interactions tested for the primary outcomes and secondary MRI outcomes. This comparison shows that combined MBSR and exercise showed no significant improvement compared with MBSR alone, exercise alone, or health education (eFigure 1 in Supplement 2).

Adherence to the Interventions and Per-Protocol Analysis

Participants had a median (IQR) attendance of 90% (80.0%-100.0%) at MBSR classes and 83.3% (71.7%-91.7%) at exercise classes in the first 6 months. eFigure 3 in Supplement 2

Table. Baseline Characteristics by Intervention Group

Characteristic	MBSR (n = 150)	Exercise (n = 138)	MBSR and exercise (n = 144)	Health education (n = 153)
Age, mean (SD), y	71.2 (4.2)	71.1 (4.9)	72.4 (5.3)	71.1 (4.6)
Sex, No. (%)				
Women	108 (72.0)	108 (78.3)	102 (70.8)	106 (69.3)
Men	42 (28.0)	30 (21.7)	42 (29.2)	47 (30.7)
Race, No. (%)				
American Indian or Alaska Native	0	1 (0.7)	1 (0.7)	0
Asian	3 (2.0)	9 (6.5)	10 (6.9)	5 (3.3)
Black or African American	18 (12.0)	14 (10.1)	18 (12.5)	19 (12.4)
Native Hawaiian or Other Pacific Islander	0	0	0	0
White	127 (84.7)	109 (79.0)	112 (77.8)	129 (84.3)
More than 1 race	1 (0.7)	0	3 (2.1)	0
Unknown/not reported	1 (0.7)	5 (3.6)	0	0
Hispanic, No. (%)	7 (4.7)	9 (6.5)	14 (9.7)	9 (5.9)
Current smoker, No. (%)	4 (2.7)	1 (0.7)	0	5 (3.3)
Education level, mean (SD), y	16.0 (2.2)	16.6 (2.2)	16.0 (2.3)	16.1 (2.1)
APOE*_E4_–positive, No. (%)	49/149 (32.9)	44 (31.9)	37/143 (25.9)	44 (28.8)
CIRS-G Score, mean (SD)[a]	6.7 (2.9)	6.7 (2.8)	6.9 (2.8)	6.7 (3.0)
Comorbidities, No. (%)				
Arthritis	69 (46.0)	73 (52.9)	67 (46.5)	63 (41.2)
Hypertension	53 (35.3)	58 (42.0)	60 (41.7)	73 (47.7)
High blood cholesterol	46 (30.7)	56 (40.6)	62 (43.1)	71 (46.4)
Credibility and expectations for improvement, mean (SD)[b]				
Credibility	30.1 (6.8) [n = 143]	33.5 (5.8) [n = 123]	32.9 (6.4) [n = 127]	26.6 (7.4) [n = 143]
Improvement	59.4 (24.2) [n = 143]	61.9 (23.5) [n = 123]	68.4 (23.0) [n = 127]	56.1 (22.5) [n = 139]
BMI classification, No. (%)[c]				
Normal (16-24.9)	57 (38.0)	34 (24.6)	35 (24.3)	47 (30.7)
Overweight (25-29.9)	51 (34.0)	51 (37.0)	63 (43.8)	54 (35.3)
Obese (≥30.0)	42 (28.0)	53 (38.4)	46 (31.9)	52 (34.0)
WTAR standard score, mean (SD)[d]	113.6 (10.6)	114.1 (10.2)	113.4 (10.4)	112.2 (10.3)
SPPB modified score, mean (SD)[e]	8.8 (1.8)	8.7 (1.9) [n = 137]	9.0 (2.0)	8.8 (2.0)
Paragraph recall score, mean (SD)				
Immediate[f]	43.0 (10.7) [n = 149]	43.4 (10.2) [n = 137]	41.9 (10.8)	42.6 (9.8)
Delayed[f]	36.4 (12.0)	37.5 (10.8)	35.8 (11.3)	36.7 (10.1)
Word List score, mean (SD)				
Learning[g]	32.4 (7.4)	31.3 (7.3)	31.2 (7.6)	31.1 (7.4)
Recall[h]	6.9 (3.1)	7.1 (3.2)	6.6 (3.0)	6.5 (3.2)

(continued)

Table. Baseline Characteristics by Intervention Group (continued)

Characteristic	MBSR (n = 150)	Exercise (n = 138)	MBSR and exercise (n = 144)	Health education (n = 153)
Neuro-QoL Cognitive Function score, mean (SD)[i]	62.4 (12.6) [n = 149]	63.2 (12.1)	65.5 (11.4)	63.3 (11.4)
OTDL score, mean (SD)[j]	20.7 (3.2)	20.3 (3.5)	20.3 (3.5)	20.2 (3.7)
CAMS-R score, mean (SD)[k]	38.1 (6.2)	37.0 (5.6)	37.8 (5.9)	36.7 (5.6)
NIH Toolbox Fluid Composite score, mean (SD)[l]	92.0 (8.7)	92.0 (10.0)	91.4 (8.4)	91.5 (9.1)
Cortisol area under curve, mean (SD)[m]	5580 (2471) [n = 134]	5703 (2606) [n = 116]	6565 (2950) [n = 123]	5749 (2500) [n = 133]
Insulin sensitivity, mean (SD)				
HOMA-IR[n]	2.5 (1.7) [n = 149]	3.0 (2.2) [n = 135]	3.0 (2.1) [n = 143]	3.1 (2.3)
OGIS, mL/min^{-1}/m^{-2}[o]	352 (61) [n = 139]	344 (63) [n = 128]	348 (67) [n = 136]	346 (67) [n = 145]

Abbreviations: MBSR, mindfulness-based stress reduction; NIH, National Institutes of Health; OTDL, Observed Tasks of Daily Living.

[a] The Cumulative Illness Rating Scale-Geriatric (CIRS-G) is a 14-item instrument that measures the number and severity of physical health problems (13 organ systems; 0-4 score for each system; overall range, 0-56). Higher scores are indicative of more comorbidities and severe medical conditions. The mean score was between 6.7 and 6.9 (dependent on the intervention group), which suggests the sample was generally healthy, with approximately 3 moderate-severity medical conditions per participant.

[b] The Credibility and Expectations Questionnaire[35] was administered after the first intervention class to evaluate participants' perception of the credibility of the intervention to which they were assigned (4 questions; score range, 4-40; higher scores indicate greater credibility), and their expectations for improvement (1 question; range, 0%-100%; higher percentages indicate expectations for greater improvement). Participants generally rated the credibility of the interventions as high, with mean ranges above 30 for all intervention groups except for health education (mean [SD] of 26.6 [7.4]). Expectations for improvement were above 50% for all groups.

[c] The percentage of people with body mass index (BMI) >30.0 in this study is slightly lower than the value reported for older adults (>60 y) of 41.5% in the National Health and Nutrition Examination Survey 2017-2020.[36]

[d] Wechsler Test of Adult Reading (WTAR) measures intelligence and has 50 items. The standard score ranges from 52 to 128, with higher scores indicating higher estimated IQ; a standard score is equivalent to an IQ score. The normative score is 100. Based on the WTAR, this sample was above-normal in terms of IQ; this aligns with the advanced educational levels.

[e] The Short Physical Performance Battery (SPPB) assesses walking speed, lower extremity strength, and balance. Modified scoring was used (range, 1-12; higher scores indicate better physical functioning). The sample had mean scores between 8.7 and 9.0, suggestive of relatively high physical functioning.

[f] The Paragraph Recall task is used to quantify memory performance. This measure involved the participant listening to 2 stories and being asked to recall and report as many of the paragraph elements as possible, with each story having 44 elements (range, 0-88 for immediate and delayed recall tests; higher scores are better). The immediate positive total mean score was slightly higher across all intervention groups (mean, 41.9-43.4) than the delayed positive total mean score (mean, 35.8-37.5).

[g] This task involved the participant recalling as many words as possible from a list of 16 words (4 learning trials were presented) (range, 0-64; higher scores are better). Across all intervention groups, the mean score was between 31.1 and 32.4, suggesting that the sample was able to recall slightly less than half of the words over the course of 4 trials.

[h] This task occurs 20 minutes from the learning task. The participant was asked to recall as many words as possible from the 16-word list (range, 0-16; higher scores are better). The mean score was between 6.5 and 7.1 across all intervention groups, suggesting that the sample was able to recall less than half of the words after the delayed period.

[i] The Quality of Life in Neurological Disorders Cognitive Function (Neuro-QoL) is an 18-item self-report measure that assess health-related quality of life (range, 18-90; higher scores are better). The mean score across all interventions was between 62.4 and 65.5, suggesting that in general participants had only mild decrements in self-reported everyday cognitive function.

[j] The Revised Observed Tasks of Daily Living measures functional capacity and has a range of 0 to 28. Higher scores suggest better functional capacity. Across all intervention groups, the mean score was between 20.2 and 20.7. This suggests high functional capacity at baseline.

[k] The self-report Cognitive and Affective Mindfulness Scale-Revised (CAMS-R) measures state mindfulness (range, 12-48; higher scores indicate greater state of mindfulness). The mean score across intervention groups ranged from 36.7 to 38.1, indicating this sample reported a high level of state mindfulness at baseline.

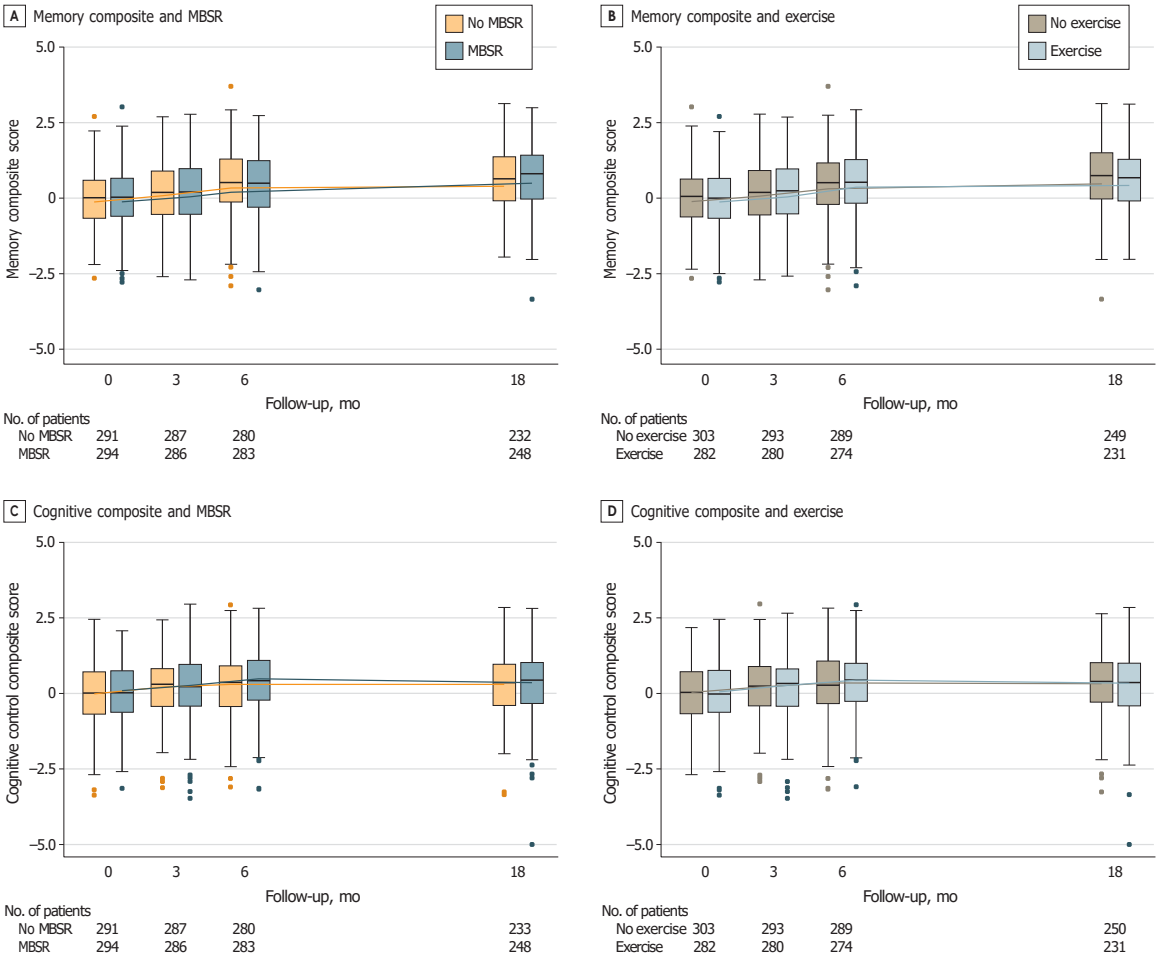
[l] This score was derived from the mean standard scores of the Flanker, Dimensional Change Card Sort, Picture Sequence Memory, List Sorting, and Pattern Comparison tasks and then deriving standard scores based on this new distribution. An uncorrected standard score at or near 100 indicates ability that is average compared with others nationally. A standard score of approximately 85 suggests significantly below-average fluid cognitive ability. The mean score of this sample was 91.4 and 92.0.

[m] Cortisol area under the curve is based on salivary measurements collected at waking, 30 minutes after waking, and bedtime on 3 consecutive days. There is no normative range for cortisol AUC for this specific assay.

[n] Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) calculated using fasting glucose and insulin. A HOMA-IR less than 1.0 indicates insulin sensitivity. The mean HOMA-IR was above 1.0 across all intervention groups.

[o] Oral Glucose Insulin Sensitivity (OGIS) calculated using a 75 g 2-hour oral glucose tolerance test obtained at the 0, 90, and 120 time points. The higher the OGIS index, the more insulin sensitive an individual is. An OGIS score of 302 mL/min^{-1}/m^{-2} (+/− 17) suggests impaired glucose tolerance. The mean OGIS score was greater than 302 mL/min^{-1}/m^{-2} across all intervention groups.

Figure 2. Memory and Executive Function Composite Changes Over 18 Months



The composite scores were the standardized mean of several neuropsychological test scores for the domain of interest. A Z score was computed for each participant ([participant score − mean]/SD), using the mean and SD of that variable computed on all randomized participants at baseline. For example, the memory composite variable was created by the mean Z scores of all available memory variables. For composite interpretation purposes, if the intervention was effective in improving each individual measure that comprised the composite by 1 SD, the overall composite score would improve by 1 point (compared with the control). The ranges for memory and executive function are −3.3 to 3.7 and −5.0 to 3.0, respectively. See eTable 2 in Supplement 2 for numerical/model data of intervention effects. The boxplot inner horizontal lines represent the median values, the boxes represent the IQR (25% and 75%), the vertical whiskers extend to the upper and lower adjacent values (the furthest points within 1.5 IQRs of the 25th and 75th percentiles), and the dots indicate outlier values.

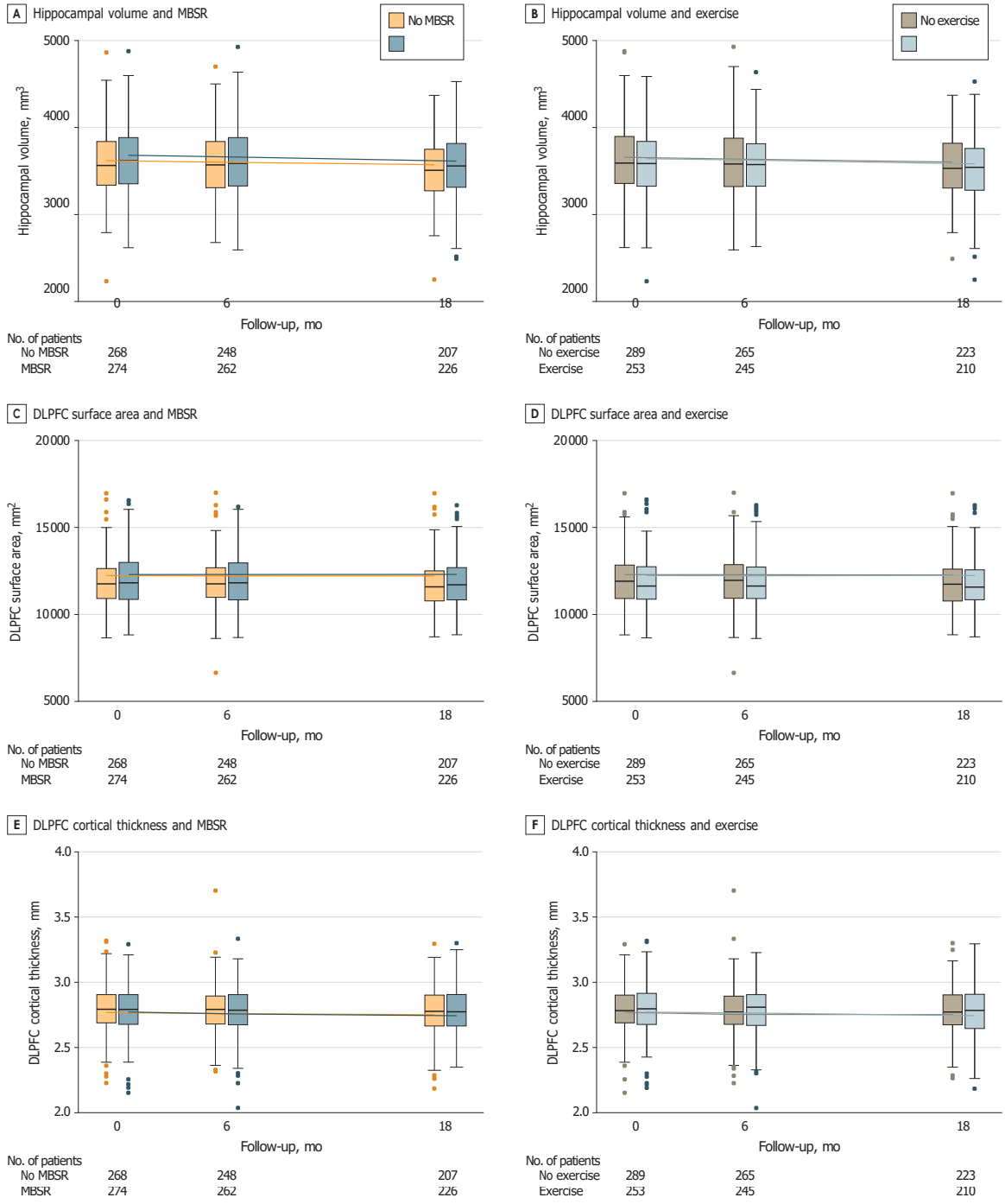
shows adherence to the interventions based on home practice and class attendance. eTable 2 in Supplement 2 compares intervention effects in the entire sample and the per-protocol subgroups; results are unchanged for all primary and secondary outcomes.

Post Hoc Analysis of Subgroups That Showed Putatively Beneficial Effects of Interventions

eTable 3 in Supplement 2 shows the effects of the interventions on multiple performance and physiological measures. Physical performance, aerobic fitness, and strength increased and sleep quality significantly improved (sleep latency was reduced and total sleep time was increased) with exercise (eTable 3A in Supplement 2). No variables were influenced by MBSR, including self-reported mindfulness (eTable 3B in Supplement 2).

Subgroups of participants who had the most change (top tertile) vs those who had the least change (bottom tertile) in these performance and physiological variables were then evaluated in terms of changes in their cognitive performance. eTable 4 in Supplement 2 quantifies these tertiles and eFigure 4 in Supplement 2 compares their episodic memory and executive function changes over 18 months. As shown in eFigure 4 in Supplement 2, there were, at most marginal, and, in the majority of cases, no differences in subgroups, which suggests limited to no evidence that MBSR or exercise

Figure 3. Structural Brain Changes Over 18 Months



Shown are the mean of the right- and left-sided brain structures. The volumes of the brain regions in this article are somewhat dependent on the measurement technique; existing literature has found that both the volumes and their rate of change are consistent with studies in healthy aging. For example, Fraser et al[37] found a rate of hippocampal atrophy of approximately 1% per year and Frangou et al[38] reported a frontal cortical thickness change of 0.005 mm per year. These are within the range of changes reported in the current sample. The ranges for hippocampal volume, DLPFC surface area, and DLPFC cortical thickness are 2232 to 4926; 6642 to 16 992; and 2.0 to 3.7, respectively. See eTable 2 in Supplement 2 for numerical/model data of intervention effects. The boxplot inner horizontal lines represent the median values, the boxes represent the IQR (25% and 75%), the vertical whiskers extend to the upper and lower adjacent values (the furthest points within 1.5 IQRs of the 25th and 75th percentiles), and the dots indicate outlier values.

differentially affected cognitive performance of participants in the top vs bottom tertiles; therefore, no inferential statistics were calculated.

Discussion

In this multicenter trial involving older adults with subjective cognitive concerns, mindfulness training, exercise, or both did not result in significant differences in improvement in episodic memory or executive function composite scores at 6 months. In secondary analyses, there were no significant improvements due to the interventions at 18 months in secondary outcomes, including structural brain measures of hippocampus and DLPFC. The findings do not support the hypothesis that these interventions improve cognitive performance in older adults.

These null findings differ from positive findings in some randomized clinical trials of exercise[29] and epidemiological data that have suggested that exercise was associated with improved cognitive and brain health in older adults,[30] as well as a smaller body of literature supporting the beneficial role of mindfulness.[31] There are several potential causes for these null findings. First, all groups showed increases in cognitive performance over time, so it could be posited that all interventions (including health education) benefited participants equally and these increases reflect those benefits, and thus the study failed due to lack of a proper negative control. Arguing against this idea is that the health education intervention was designed for this study so that it would not specifically target cognition (eg, it did not include a mindfulness or exercise regimen). Further, if cognitive performance increases represented true benefits, one would expect to see a reflection of those benefits in brain structures (ie, increase or attenuated decrease in the size of hippocampus and DLPFC, structures involved in episodic memory, and executive function), yet both structures showed longitudinal declines with all conditions, consistent with age-related atrophy not attenuated by the interventions. In addition, the combination of MBSR and exercise showed no greater change than each intervention alone. Thus, the increases in cognitive performance likely reflect expectancy or practice effects from repeated exposure to the assessments.

Another potential cause of the null findings was failure in target engagement (ie, failure in having the desired effect from the interventions), which could result from poor participant adherence, low intervention fidelity by instructors, low intensity of interventions, or low reliability of outcome measures. However, none of these problems were apparent: participants demonstrated high adherence and retention in the study, instructors were trained and supervised for fidelity, the intensity of interventions was similar to that in prior trials, and outcome reliability was good. Furthermore, per-protocol analyses of participants that were more highly adherent to the interventions showed no significant differences from the overall sample. In the exercise intervention, physiological and performance changes suggest participants benefited from exercise. Thus, the findings are similar to the Lifestyle Interventions and Independence for Elders Study, which showed a beneficial effect of 24 months of exercise on disability prevention, but not cognitive performance.[32] In contrast, MBSR was not associated with significant change in any physiological or performance measure, which raises the question of whether the implementation of MBSR was sufficient; however, given adequate instructor fidelity, participant class attendance, and home practice, the lack of a measurable effect of mindfulness training may reflect a lack of clearly-measurable targets in mindfulness-based intervention.

Another possibility accounting for lack of detectable effect of interventions is that participants were generally healthy and potentially insufficiently sedentary at baseline, thereby limiting potential for benefiting from lifestyle interventions. To test this, subgroup analyses of those who showed the greatest changes in physiological or performance variables posited to underlie cognitive health (eg, improved insulin sensitivity) were conducted. These analyses found that, even when the interventions produced beneficial changes in these putative mechanisms, they still did not lead to significant cognitive benefits. Thus, the health of the participants does not appear to explain the null results. As a whole, these results suggest that the underlying hypothesis is unsupported.

Limitations

This study has several limitations. First, the participants were largely White and the majority were college-educated; this limited diversity reduces generalizability of findings. Second, the study focused on structural characteristics of hippocampus and DLPFC as proxy measures of the brain's health; other regions or assessment techniques might be more sensitive to intervention effects.[33] Third, the study tested interventions over 18 months; a longer period of intervention may be needed to show beneficial effects. Fourth, the study focused on healthy older adults who were objectively cognitive intact; some studies have found beneficial effects of exercise on cognitive function in more physically or cognitively ill and frail older adults,[34] as well as benefits of MBSR in older adults with depression and anxiety.[7] Fifth, individuals with subjective cognitive concerns are a heterogeneous group that could include those with incipient dementia as well as individuals experiencing the influence of medications, medical conditions, or nutrition status. These and other potentially remediable mechanisms beyond cortisol, insulin sensitivity, and aerobic fitness were not examined in this study and should be considered in future research.

Conclusions

Among older adults with subjective cognitive concerns, mindfulness training, exercise, or both did not result in significant differences in improvement in episodic memory or executive function composite scores at 6 months. The findings do not support the use of these interventions for improving cognition in older adults with subjective cognitive concerns.

ARTICLE INFORMATION

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Other - Served as Research Coordinator for study: Voegtle.
Other - Design, implementation, and evaluation of exercise intervention: Nichols.
Other - Data analysis concerning insulin kinetics and sensitivity: Patterson.

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Neurobiology of Disease

Integrity of Neuronal Size in the Entorhinal Cortex Is a Biological Substrate of Exceptional Cognitive Aging

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Average aging is associated with a gradual decline of memory capacity. SuperAgers are humans ≥80 years of age who show exceptional episodic memory at least as good as individuals 20–30 years their junior. This study investigated whether neuronal integrity in the entorhinal cortex (ERC), an area critical for memory and selectively vulnerable to neurofibrillary degeneration, differentiated SuperAgers from cognitively healthy younger individuals, cognitively average peers ("Normal Elderly"), and individuals with amnestic mild cognitive impairment. Postmortem sections of the ERC were stained with cresyl violet to visualize neurons and immunostained with mouse monoclonal antibody PHF-1 to visualize neurofibrillary tangles. The cross-sectional area (i.e., size) of layer II and layer III/V ERC neurons were quantified. Two-thirds of total participants were female. Unbiased stereology was used to quantitate tangles in a subgroup of SuperAgers and Normal Elderly. Linear mixed-effect models were used to determine differences across groups. Quantitative measurements found that the soma size of layer II ERC neurons in postmortem brain specimens were significantly larger in SuperAgers compared with all groups ($p < 0.05$)—including younger individuals 20–30 years their junior ($p < 0.005$). SuperAgers had significantly fewer stereologically quantified Alzheimer's disease-related neurofibrillary tangles in layer II ERC than Normal Elderly ($p < 0.05$). This difference in tangle burden in layer II between SuperAgers and Normal Elderly suggests that tangle-bearing neurons may be prone to shrinkage during aging. The finding that SuperAgers show ERC layer II neurons that are substantially larger even compared with individuals 20–30 years younger is remarkable, suggesting that layer II ERC integrity is a biological substrate of exceptional memory in old age.

Key words: Alzheimer's disease; entorhinal cortex; neurofibrillary tangles; neuronal integrity; SuperAging

Significance Statement

Average aging is associated with a gradual decline of memory. Previous research shows that an area critical for memory, the entorhinal cortex (ERC), is susceptible to the early formation of Alzheimer's disease neuropathology, even during average (or typical) trajectories of aging. The Northwestern University SuperAging Research Program studies unique individuals known as SuperAgers, individuals ≥80 years old who show exceptional memory that is at least as good as individuals 20–30 years their junior. In this study, we show that SuperAgers harbor larger, healthier neurons in the ERC compared with their cognitively average same-aged peers, those with amnestic mild cognitive impairment, and – remarkably – even compared with individuals 20–30 years younger. We conclude that larger ERC neurons are a biological signature of the SuperAging trajectory.

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Introduction

Memory capacity declines during the course of average aging. The entorhinal cortex (ERC) and hippocampus, two areas critical for episodic memory, are selectively susceptible to neurofibrillary tangle (NFT) formation. This phenomenon starts as an age-related process and intensifies in a prodromal stage of Alzheimer's disease (AD), known as amnestic mild cognitive impairment (aMCI), reaching its peak in the dementia of AD. Even age-related memory decline could therefore reflect the emergence of neurofibrillary degeneration in the hippocampus and entorhinal cortex (Balasubramanian et al., 2012; Koen and Yonelinas, 2016; Gefen et al., 2018). While this age-related decline is common, it is not necessarily inevitable.

The Northwestern University SuperAging Research Program investigates a unique trajectory that reflects the resistance and resilience to the involutional process characteristic of the MCI–AD continuum. SuperAgers (SAs) are defined as individuals ≥80 years old who demonstrate episodic memory performance at least as good as what would be considered normal for individuals 20–30 years younger (Harrison et al., 2012; Rogalski et al., 2013; Gefen et al., 2014). Of the first 10 cases that came to autopsy, the hippocampus and ERC contained a low to intermediate density of NFTs (Braak stages II–III), whereas healthy cognitively average age-matched control subjects ("Normal Elderly") had an NFT density range that extended into Braak stage IV (Merrill et al., 2000; Rogalski et al., 2019). Even the NFT-containing limbic areas in SuperAgers contained many healthy-appearing neurons and the neocortex was generally free of neurofibrillary degeneration (Rogalski et al., 2019). The status of ERC neurons is of particular interest in light of the exceptional memory performance in SuperAgers despite old age. A central question is whether SuperAgers are resistant to neurofibrillary degeneration or are resilient to the effects of NFT on neuronal number and size.

Prior research has shown that the number of cortical neurons does not display age-related changes in cognitively intact elderly free of dementia (Stark et al., 2007; Freeman et al., 2008). Recent work on postmortem cases with non-AD dementia demonstrated a tight concordance between shrinkage of neuronal soma and the manifestation of clinical symptoms (Kim et al., 2018). In an effort to understand the factors that contribute to the preservation of memory and to the SuperAging phenotype, the current study investigated the cross-sectional area (i.e., size) of neurons in the ERC in a rare series of autopsies. Stellate cells in layer II and pyramidal cells in layer III/V of the ERC were targeted for measurement given their pivotal role in the reciprocal transfer of information between association cortex and the hippocampal formation (Van Hoesen and Hyman, 1990; Van Hoesen and Solodkin, 1993; Canto et al., 2008), their position along the perforant pathway (Hyman et al., 1984, 1986; Witter, 2007), and the relative paucity of ERC NFTs in SuperAgers compared to their cognitively average peers (Gefen et al., 2021). Stereological quantitation was also performed in a subset of specimens to determine the relationship between NFT formation and neuronal size in layer II of the ERC. The result of this investigation includes the unexpected finding that ERC neuronal size is significantly larger in SuperAgers compared with younger neurologically healthy individuals, in addition to their same-aged elderly peers. This outcome raises fundamental questions regarding the nature of the age-related involutional phenomena in SuperAgers and their relationship to superior memory capacity.

Materials and Methods

Participant characteristics

All participants were required to demonstrate preserved activities of daily living. All participants were also required to lack clinical evidence or history of neurologic or psychiatric disease. The autopsied brains of six participants characterized as "Cognitive SuperAgers" from the Northwestern University SuperAging Research Program were identified from the Northwestern University Alzheimer's Disease Research Center Brain Bank. As comparison, the autopsied brains of seven "cognitively average elderly" ["Normal Elderly"(NE)] participants from the Northwestern University SuperAging Research Program, six healthy younger adults ["Younger Controls" (YCs)], and five participants with antemortem aMCI were additionally identified. Written informed consent and agreement to enter the brain donation program were obtained from all participants in the study, and the study was approved by the Northwestern University Institutional Review Board and in accordance with the Helsinki Declaration (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/). Samples from representative brain regions of each participant were surveyed qualitatively and found to be free of significant neurodegenerative pathology other than amyloid plaques and neurofibrillary tangles. Braak staging (Braak and Braak, 1991b; Braak et al., 1993) was surveyed in each participant to identify the degree of tangle involvement. Apolipoprotein E (ApoE) genotype was assessed using DNA extracted from blood samples provided by each participant according to enrollment procedures into the Northwestern University SuperAging Research Program. See Table 1 for participant characteristics.

Inclusion criteria

Cognitive SuperAgers. Detailed inclusion criteria have been reported previously (Rogalski et al., 2013). Briefly, all participants were community-dwelling, English-speaking adults ≥80 years of age who were free of significant neurologic or psychiatric illness. Inclusion criteria also included neuropsychological test performance criteria, which were chosen for their relevance for cognitive aging and their sensitivity to detect clinical symptoms associated with dementia of the Alzheimer's type (Weintraub et al., 2009). The delayed recall score of the Rey Auditory Verbal Learning Test (RAVLT; Schmidt, 2004) was used as a measure of episodic memory, and SuperAgers were required to perform at or above average normative values for individuals in their 50s and 60s (midpoint age, 61 years; RAVLT delayed recall raw score, ≥9; RAVLT delayed recall scaled score, ≥10; for more information, see Gefen et al., 2015).

Cognitively average Normal Elderly individuals. Cognitively average elderly individuals were community-dwelling, English-speaking adults ≥80 years of age who were free of significant neurologic or psychiatric illness and were enrolled into the Northwestern University SuperAging Research Program as cognitively average control subjects based on neuropsychological performance. Specifically, these individuals were required to fall within 1 SD of the average range for their age and education before death (Ivnik et al., 1996; Heaton et al., 2004; Shirk et al., 2011). Criteria are in accordance with the National Institute on Aging and Alzheimer's Association (NIA-AA) for elderly individuals considered "not demented" (Albert et al., 2011).

Younger cognitively average individuals (Younger Controls). Ages of the younger cognitively average participants ranged from 26 to 61 years. Clinical records were available for each participant and were assessed carefully for evidence of cognitive deficits. If the clinical history did not definitively validate normal cognitive function, this information was obtained from the next of kin.

Individuals with aMCI diagnosis. Participants received a diagnosis of aMCI during life based on the criteria proposed by the NIA-AA (Albert et al., 2011). Individuals with an antemortem diagnosis of aMCI were required to show clear impairment on neuropsychological tests of memory and no impairment in other cognitive domains.

Tissue processing and histopathology

Postmortem intervals (PMIs) ranged from 3 to 58 h. After autopsy, each specimen was cut into 3–4 cm coronal blocks and fixed in 4%

Table 1. Participant characteristics

Participant	Age at death (years)	Sex	Education (years)	PMI (h)	Brain weight (g)	Braak staging	ApoE	Non-AD pathology
SA 1	99	F	16	58	1020	III	3, 3	Multiple cortical microinfarcts (nonsignificant); 1 remote lacunar infarct, left putamen; ARTAG, AGD
SA 2	90	F	18	4	990	III	3, 3	ARTAG, AGD, 1 remote lacunar infarct, left globus pallidus
SA 3	90	F	14	4.5	1100	II-III	2, 3	PART (definite), Lewy body in dorsal motor nucleus of vagus (incidental), ARTAG
SA 4	95	F	18	5	1241	0	NA	NA
SA 5	92	M	16	11	1247	I	3, 3	Medial temporal TDP-43 pathology; moderate cerebrovascular disease, non-occlusive
SA 6	82	F	14	24	1241	I	3, 3	Lewy bodies in substantia nigra and locus coeruleus, incidental; mild cerebrovascular disease, nonocclusive
NE 1	96	F	14	5	NA	IV	NA	NA
NE 2	88	M	12	12	1250	III-IV	NA	NA
NE 3	82	M	NA	24	NA	III-IV	NA	NA
NE 4	95	F	12	3.25	1096	III	2, 3	NA
NE 5	89	F	16	9	1180	II	3 ,3	NA
NE 6	88	M	20	9	1490	I	3, 3	Glioblastoma, WHO grade IV, 9.0 cm in greatest dimension, left parieto-occipital region; amygdala-only Lewy body disease
NE 7	87	F	16	16	1183	I	3, 3	Moderate vascular disease
aMCI 1	89	F	18	4.5	1280	II	NA	None
aMCI 2	99	F	13	5	1060	III-IV	3, 3	None
aMCI 3	92	F	12	3.5	1084	III-IV	3, 3	None
aMCI 4	90	M	14	3	1380	III	3, 3	None
aMCI 5	92	M	16	4.5	1100	V	3, 4	Superficial contusion in occipital lobe
YC 1	45	M	NA	13	1650	0	NA	NA
YC 2	61	F	NA	22	1080	I	NA	NA
YC 3	50	F	NA	48	1150	0	NA	NA
YC 4	57	F	NA	6	1100	0	NA	NA
YC 5	59	F	NA	20	1300	NA	NA	NA
YC 6	26	M	NA	8	1560	0	NA	NA

ARTAG, aging-related tau astrogliopathy; AGD, argyrophilic grain disease; PART, primary age-related tauopathy; CHD, coronary heart disease; NA, not available; F, female; M, male; WHO, World Health Organization; None, TDP-43 staining was not available. Braak staging followed published guidelines (Braak and Braak, 1985, 1991a,b; Braak et al., 1993).

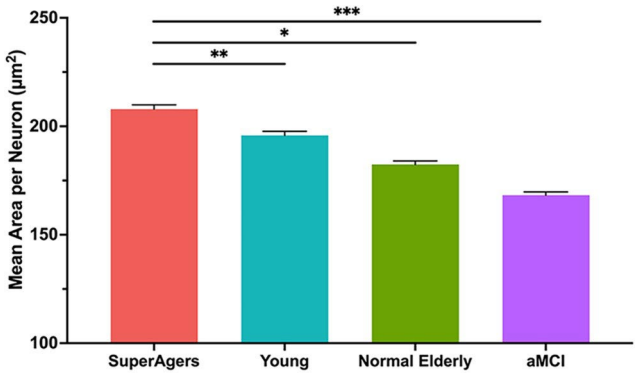

Figure 1. Mean cross-sectional area per neuron in layer II of the entorhinal cortex. Heights of bars represent the difference in mean cross-sectional area per squared micrometer of layer II neurons in the entorhinal cortex between SuperAgers ($N = 6$), Younger Controls ($N = 6$), Normal Elderly ($N = 7$), and individuals with aMCI ($N = 5$). An overall average of ; 1044 neurons (SD, 229) were measured per group. SuperAgers showed a significantly larger mean area of layer II ERC neurons compared with Normal Elderly, aMCI individuals, and Younger Controls. There were no significant differences in the mean area of layer II neurons between Normal Elderly, aMCI individuals, and Younger Controls. Statistical significance was assessed using a linear mixed-effect model. Error bars represent the SEM. *p , 0.05; **p , 0.01; *** p , 0.001.

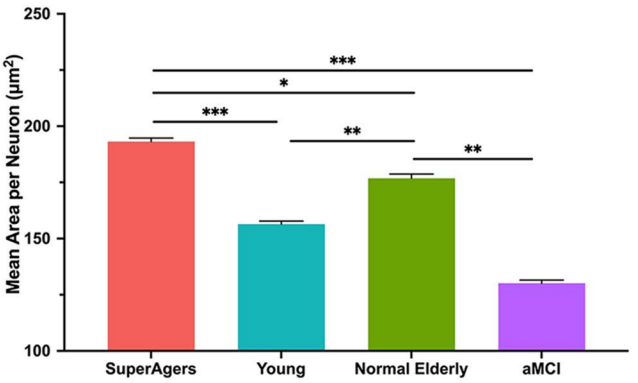

Figure 2. Mean cross-sectional area per neuron in layer III/IV of the entorhinal cortex. Heights of bars represent the mean cross-sectional area per square micrometer of layer III/V neurons in the entorhinal cortex among SuperAgers ($N = 6$), Younger Controls ($N = 6$), Normal Elderly ($N = 7$), and individuals with aMCI ($N = 5$). An overall average of ; 1052 neurons (SD, 53) were measured per group. Mean area of layer III/V ERC neurons was significantly larger in SuperAgers compared with Normal Elderly, aMCI individuals, and Younger Controls. Normal Elderly also showed larger neuronal cross-sectional area in layer III/V of the ERC compared with aMCI individuals and Younger Controls. Statistical significance was assessed using a linear mixed-effect model. Error bars represent the SEM. *p , 0.05; **p , 0.01; ***p , 0.001.

paraformaldehyde for 30–36 h at 4°C, and then taken through sucrose gradients (10–40% in 0.1 M sodium phosphate buffer, pH 7.4) for cryoprotection and stored at 4°C. Blocks were sectioned at a thickness of 40 μm on a freezing microtome and stored in 0.1 M phosphate buffer containing 0.02% sodium azide at 4°C until use. Regions were equivalent across tissue blocks taken from the anterior entorhinal cortex. Up to six sections (intersection interval, 24 or 54) of the entorhinal cortex were collected, and a 1.0% cresyl violet Nissl stain was used to visualize neurons. All specimens were evaluated grossly for cortical, caudate, cerebellar, and brainstem atrophy, as well as vascular pathology. Braak staging (Braak et al., 1993) was surveyed in each case to identify NFT involvement in transentorhinal/entorhinal cortex, other limbic cortical areas, and neocortical regions. SuperAger, Normal Elderly, and aMCI specimens were also evaluated microscopically for Lewy and non-Lewy α-synucleinopathies, vascular pathologies, frontotemporal lobar degeneration-tau, and pathologic TDP-43 (Table 1).

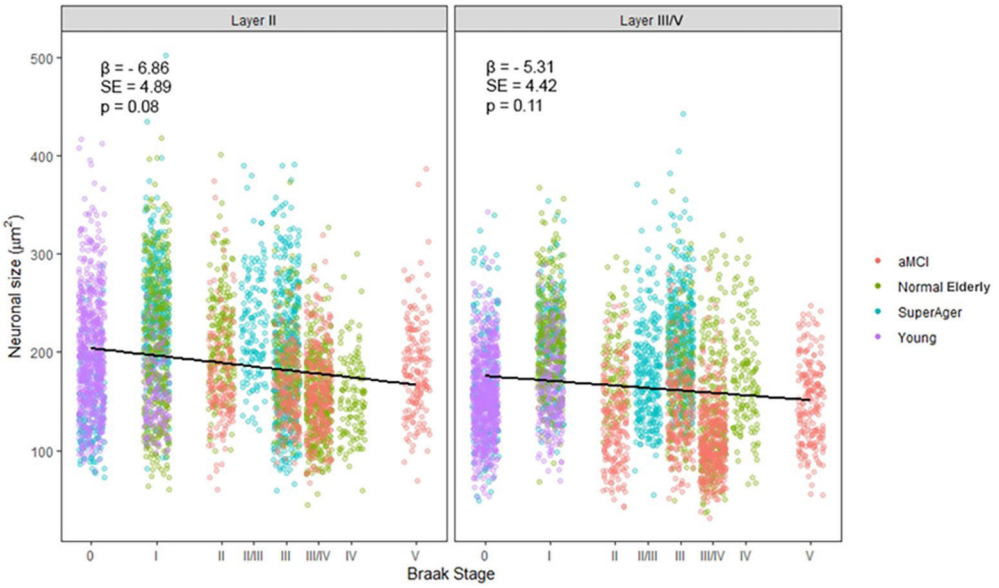

Figure 3. Relationship between the cross-sectional area of layer II ERC neurons and Braak stage. Moderate evidence for a negative association of increasing Braak stage on neuronal cross-sectional area (in μm^2) was found, yet it did not quite reach statistical significance in ERC layer II ($p = 0.08$; $b = 6.86$) and in ERC layer III/V ($p = 0.11$; $b = 5.31$). Statistical significance was assessed using a linear mixed-effect model. b, Regression coefficient; SE, SE of the regression coefficient.

Measurement of cross-sectional area of neurons in the ERC

The cross-sectional area of neurons in layer II and layer III/V of each ERC region per participant was measured. Layer II neurons were identified by their stellate appearance and their arrangements in islands of neurons. Layer III/V neurons were identified by their pyramidal shape and the orientation of their apical dendrite toward the cortical surface. To measure the cross-sectional area of neurons, 6–10 photomicrographs were obtained randomly from sections spanning layer II and layer III/V per each ERC layer and analyzed at 20× magnification. Analysis of the cross-sectional area of neurons in the ERC was conducted by an individual blinded to group affiliation; a second rater performed analyses of the area of ERC neurons on three cases to ensure consistency in measurement. Analysis was conducted using the image analysis software ImageJ (version 1.53). Within ImageJ (RRID:SCR_003070), the tracing function was used to measure the area of the neuron at 5.5 pixels/μm (image size, 1600 × 1200 pixels). The area was obtained for at least 100 neurons per layer (II and III/V independently) of the ERC region per participant. Mean total area of neurons was calculated in layer II and layer III/V of the ERC, per case, and evaluated for differences across groups.

Modified stereological analysis of NFT pathology in layer II of ERC

In a subset of cases (five SuperAgers and five Normal Elderly) with tissue available, modified stereological methods were used to estimate the density of PHF-1-stained tangles in layer II. Thioflavin-S-positive NFT counts in the ERC without specific quantitation of laminar patterns are reported in the study by Gefen et al. (2021). Whole-hemisphere sections were selected that contained ERC with clear layer II cell islands and were immunostained with the mouse monoclonal antibody PHF-1 (P. Davies, Albert Einstein College of Medicine, New York, NY; catalog #PHF1; RRID:AB_2315150). PHF-1 recognizes tau phosphorylated at Ser396/404 and allows for visualization of tangles and pretangles in the ERC. Briefly, layer II of the ERC was traced at 2.5× magnification and analyzed at 40× magnification by an individual blinded to group. Analysis was performed using the fractionator method and StereoInvestigator software (MBF Bioscience; RRID:SCR_004314). The sections used in analysis were treated as adjacent sections, allowing for calculation of the density in the total volume within the sections. The top and bottom 10 μm of each section were set as the guard height. The dimensions of the counting frame chosen were 225 × 225 μm, based on trials. The coefficient of error was calculated, and sampling parameters were adjusted so that the coefficient of error was ≤0.1. Data were expressed as counts per cubic millimeter based on planimetric calculation of volume by the fractionator software. Mean NFT densities were compared between the two groups.

Experimental design and statistical analysis

The study used a cross-sectional experimental design based on autopsied specimens. A Kolmogorov–Smirnov test for equality of distributions was used to confirm consistency between two raters of neuronal size. The test failed to reject the null hypothesis of equal distributions, indicating agreement (i.e., consistency) between raters. Differences among age at death, education, and PMI were determined using a one-way ANOVA. A linear mixed-effect model with a random intercept for subject was used to compare the mean neuronal cross-sectional area among the four groups for layer II and layer III/V. The same model was used to determine differences in area between layer II and layer III/V neurons across all cases. Postmortem interval, age at death, and Braak stage, were included as covariates. The p-value for rejecting the null hypothesis was set at 0.05. Linear mixed-effect modeling was also used to test whether there was an association among age at death, cross-sectional area of neurons, and Braak staging (layer II and layer III/V, independently). Braak staging was treated as a continuous variable. Statistical analyses were performed using RStudio Software (version 4.0.3; RRID:SCR_000432). A Welch's t test was used to compare the densities of NFTs in layer II between SuperAgers and Normal Elderly.

Results

In accordance with criteria, the mean age of Younger Controls (mean age, 49.67 years; SD, 13.05) was significantly lower than those of SuperAgers (mean age, 91.33 years; SD, 5.72), Normal Elderly (mean age, 89.29 years; SD, 4.82), and aMCI (mean age, 92.40 years; SD, 3.91; p < 0.05); there were no significant differences in age among other groups. No group differences were found among years of education, PMI, or brain weight. Only one aMCI case (aMCI 5) carried an APOE-4 allele, a known risk factor for Alzheimer's disease (Saunders et al., 1993; Roses, 1996). The Braak staging of NFTs in aMCI subjects ranged from II to V, in Normal Elderly from I to IV, and in SuperAgers from 0 to III. All Younger Controls showed a

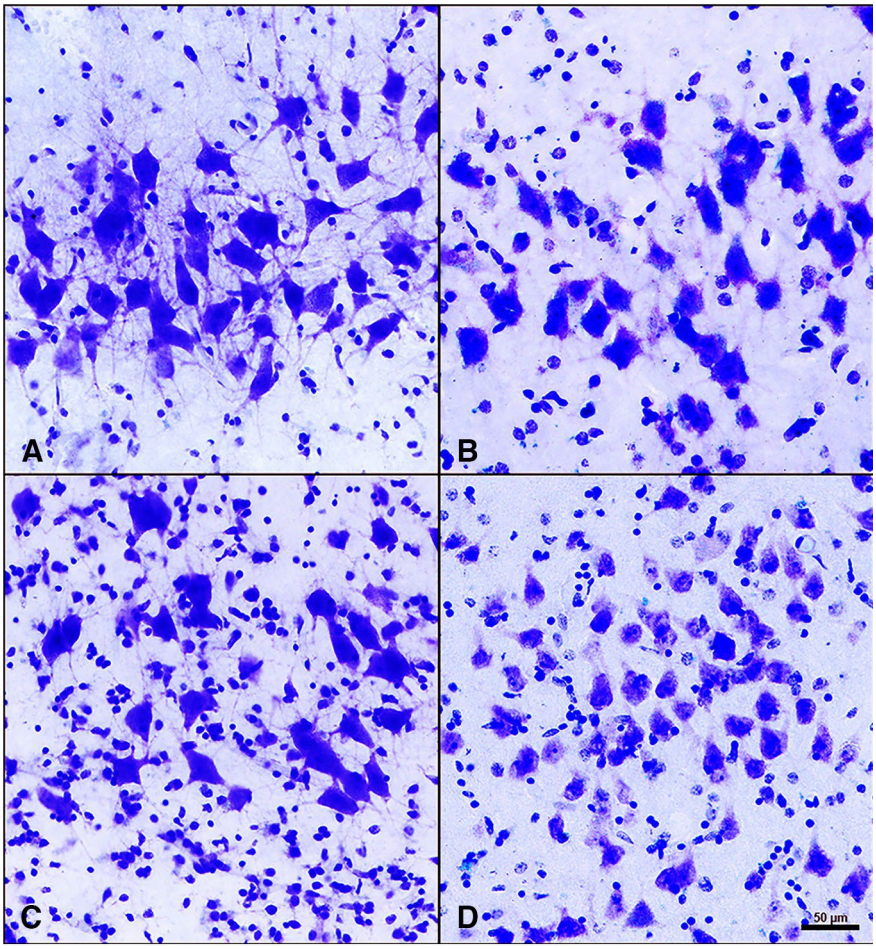

Figure 4. Layer II neurons of the entorhinal cortex in SuperAgers, Younger Controls, Normal Elderly, and aMCI individuals. *A–D*, Layer II neurons in SuperAgers, Younger Controls, Normal Elderly, and individuals with aMCI visualized with cresyl violet staining. *A*, SA 2, a 90-year-old female SuperAger. *B*, YC 4, a 57-year-old female young control subject. *C*, NE 6, an 88-year-old male elderly control subject. *D*, aMCI 1, an 89-year-old female with aMCI. Scale bar: (in *D*) *A–D*, 50 μm. *A–D*, SuperAger (*A*) shows a significantly larger mean area of layer II ERC neurons compared with Younger Controls (*B*), Normal Elderly (*C*), and individual with aMCI (*D*).

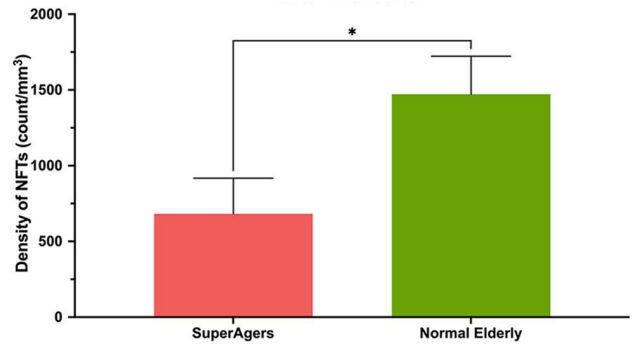

Figure 5. Density of NFTs in layer II of the entorhinal cortex heights of bars represent the mean density per cubic millimeter of NFTs in layer II neurons in the entorhinal cortex between SuperAgers ($N = 5$) and Normal Elderly ($N = 5$). Density of NFTs in layer II ERC neurons was significantly smaller in SuperAgers (mean, 682; SEM, 235) compared with Normal Elderly (mean, 1472; SEM, 251; p , 0.05). This relationship held when controlled for Braak staging. Statistical significance was assessed using a Welch's *t* test. Error bars represent the SEM.

Braak stage of 0 with the exception of participant "YC 2" (stage I; Table 1).

For each group, the mean cross-sectional area of neuronal soma was significantly greater in layer II compared with layer III/V (SuperAgers, Younger Controls, aMCI: p , 0.001; Normal Elderly: $p = 0.005$). Mean soma area of layer II ERC neurons was significantly larger in SuperAgers compared with Normal Elderly (p , 0.05), aMCI individuals ($p = 0.001$), and, remarkably, Younger Controls (p , 0.005). There were no significant differences in the mean area of neurons among Normal Elderly, Younger Controls, and aMCI individuals in layer II of the ERC [Fig. 1 (see also Fig. 4)]. At the individual-case level, there was some overlap in layer II soma sizes, highlighting variability; for example, two SuperAgers (SA 1 and SA 4) showed soma sizes that fell below the average size of their same-age peers, and the inverse was true for two Normal Elderly (NE 5 and NE 6). The mean area of layer III/V ERC neurons followed the same trend, where SuperAgers showed a larger soma area than Normal Elderly (p , 0.05), Younger Controls (p , 0.001), and aMCI individuals (p , 0.001). However, Normal Elderly showed a significantly larger soma area of layer III/V neurons compared with aMCI individuals ($p = 0.003$) and, unexpectedly, Younger Controls ($p = 0.01$). This is also likely because of the presence of variability in soma size among individual cases given the small groups of postmortem brain tissue, particularly in the Normal Elderly (Fig. 2).

Analyses were performed to determine whether there was a relationship between age at death and the cross-sectional area of neurons within layer II and layer III/V of the ERC, regardless of group affiliation. There was no evidence of an association between age at death and area of layer II and III/V neurons of the ERC. The same relational analyses were performed to determine the relationship between cross-sectional area of neurons and Braak staging (Figs. 3, 4). There was moderate evidence for a negative association of increasing Braak stage on neuronal cross-sectional area that did not quite reach statistical significance in layer II ($p = 0.08$; $b = 6.86$) or layer III/V ($p = 0.11$; $b = 5.31$) of the ERC.

Finally, modified unbiased stereology was performed in ERC sections stained immunohistochemically with PHF-1 to visualize layer II pre-NFTs and mature NFTs in a subset of five SuperAgers (SA 1–5) and five Normal Elderly (NE 1, 2, 3, 6, and 7). The estimated PHF-1-positive NFT densities in layer II were significantly higher in Normal Elderly (; 1500/mm³) compared with SuperAgers (; 700/mm³; p , 0.05), by a difference of about twofold (Figs. 5, 6).

Discussion

Cognitive SuperAgers are individuals 2: 80 years of age who appear to be resistant to the deleterious effects of aging on memory function. Thus far, prior research reported that compared with same-aged peers, SuperAgers show less white matter neuroinflammatory markers (Gefen et al., 2019) and acetylcholinesterase activity (Janeczek et al., 2018), higher cortical volumes (Harrison et al.,

2012; Rogalski et al., 2013; Sun et al., 2016), lower rates of atrophy (Cook et al., 2017), and higher density of Von Economo neurons in the anterior cingulate cortex (Gefen et al., 2018) when compared with Normal Elderly. Additional neuropathologic studies of successful agers found associations between preservation of cognition and decreased levels of neurofibrillary tangles (Kawas et al., 2015), amyloid plaques (Kawas et al., 2021), and TDP-43 inclusions (Nelson et al., 2022) in postmortem samples. In a recent study, we reported that SuperAgers harbor fewer NFTs in the entirety of the ERC compared with Normal Elderly and individuals with aMCI (Gefen et al., 2021). The current study extended these findings through an examination of neuronal size as a proxy for cellular integrity of the ERC in SuperAgers. There were four novel findings. First, SuperAgers displayed significantly larger neuronal cross-sectional area in layer II of the ERC when compared with Normal Elderly, individuals with aMCI, and, most remarkably, even relative to the mean ERC cell size of Younger Controls, some of whom were nearly 60 years their junior. Second, a small to moderate negative effect was found between age at death and neuronal size in layer II among all cases, a trend that was recapitulated by the relationship between Braak stage and size as well. Third, we found that SuperAgers harbored significantly fewer NFTs in layer II alone than Normal Elderly. Finally, and in accordance with prior literature (Krimer et al., 1997; Merrill et al., 2000), within the ERC and across all groups, layer II perikarya were larger than those that dwell in layer III/V. Taken together, we can conclude that the integrity of neuronal size in the entorhinal cortex is a biological substrate of exceptional cognitive aging. The inverse is also true: that is, neuronal atrophy appears to be a characteristic marker of normal and pathologic aging. We suspect that this process is a function of neurofibrillary formation in the affected cells (Fig. 7), leading to compromised memory abilities in older age.

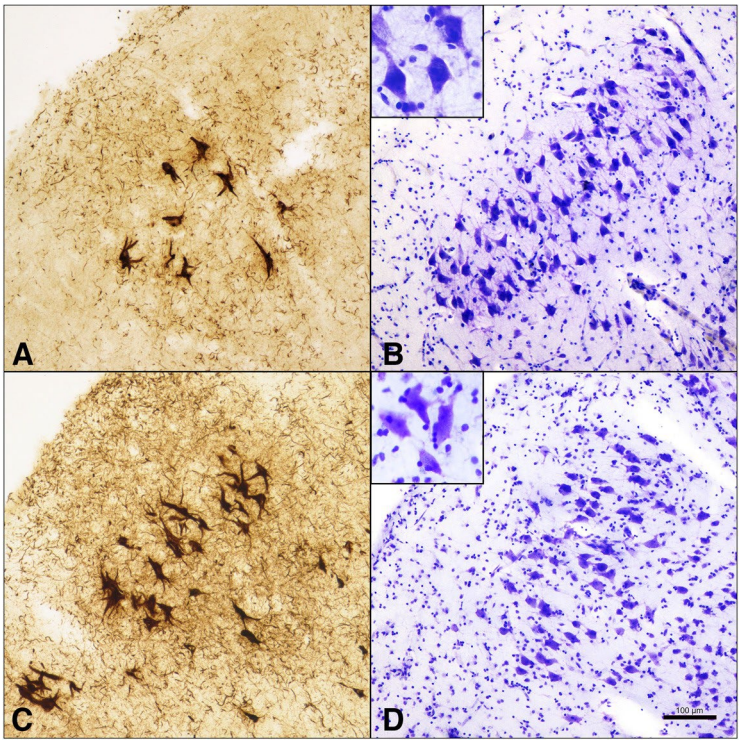

Figure 6. NFTs in layer II ERC neurons compared with neuronal size in SuperAgers and Normal Elderly. *A*, *B*, SA 2, a 90-year-old female SuperAger. *C*, *D*, NE 6, an 88-year-old male elderly control. SuperAger shows significantly fewer layer II NFTs (*A*) and larger layer II soma size (*B*) compared with Normal Elderly (*C*, *D*). Scale bar, 100 µm.

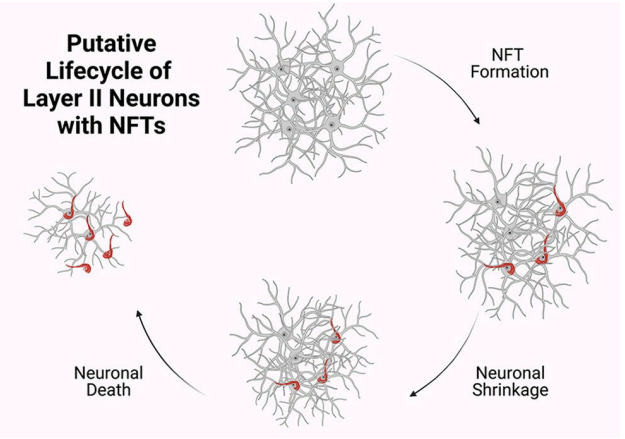

Figure 7. Putative life cycle of layer II neurons with NFTs. Results suggest that in stellate neurons in layer II of ERC, NFT formation leads to neuronal shrinkage. As previously understood, NFTs undergo biochemical changes and remain as "ghost tangles" after their associated neurons dies. Neuronal shrinkage may be an initial mechanism along the course toward age-related cognitive impairment. Created with BioRender.com.

For reasons that remain unknown, cell populations in the ERC are selectively vulnerable to NFT formation during normal aging and in early stages of AD (Braak and Braak, 1985, 1991a). In contrast, SuperAgers either resist the neuropathologic changes of aging and AD or are resilient to cognitive impairment despite demonstrating pathologic brain changes (Rogalski et al., 2013, 2019; Gefen et al., 2021). In a previous report, despite an overlap in Braak staging, NFT burden in SuperAgers was unusually low in the ERC given their age with approximately three times fewer NFTs compared with Normal Elderly across the entire ERC (Gefen et al., 2021). In the current study, Braak staging ranged from 0 to III in SuperAgers and from I to IV in Normal Elderly, again with overlap. When viewed in relation to layer II cell size, there was evidence to suggest that increased NFT pathology is a biological driving force leading to neuronal shrinkage. This was most apparent in the aMCI group, where AD is pathologically present and cell size is significantly lower compared with other groups. To our knowledge, this is one of the first reports to suggest that neuronal shrinkage is a biological substrate of NFT degeneration and poor memory functioning. Current findings showing that SuperAgers resist layer II NFTs in the ERC strongly suggest that a neuron spared from tangle formation can maintain its structural integrity. The remarkable observation that SuperAgers showed larger layer II neurons than their younger peers may imply that large ERC stellate cells were present *de novo* and are maintained structurally throughout life.

Future in-depth studies are needed to examine possible mechanisms of neuronal, axonal, synaptic, and dendritic integrity in larger samples of SuperAgers across corticolimbic regions. The nucleus basalis of Meynert, for example, contains a population of

cholinergic neurons (Ch4) that are distinctly magnocellular, and project to the olfactory bulb, the amygdala, and the entire cortical mantle (Mesulam et al., 1983). Early pretangles form first in Ch4 neurons in parallel with layer II neurons of the ERC over the course of aging and AD, then spread to other limbic/paralimbic areas, then to neocortex. The cause of vulnerability is not presumed to be the cholinergic nature of Ch4 but rather its location within a continuous band of limbic structures (Mesulam, 2013). The investigation of dendritic and axonal integrity, synaptic abnormalities, and genetic and metabolomic factors in any of these anatomically vulnerable limbic regions are all viable avenues of exploration. In the hippocampus proper, synaptic loss in particular is highly correlated with cognitive decline in AD (Honer et al., 1992; Colom-Cadena et al., 2020). Such decline is thought to be because of the loss of afferents from layer II ERC neurons that span to the outer molecular layer of the dentate gyrus (Scheff et al., 2006). In animal models of successful aging, the preservation of postsynaptic densities in the molecular layer correlated with better spatial learning ability in cognitively intact rats (Smith et al., 2000; Morrison and Baxter, 2012). Less is known, however, about the status of synaptic integrity in limbic systems in human specimens procured from successful agers. A fruitful future study involves the measurement of synaptic proteins in layer II pyramidal neurons and throughout hippocampal subfields to establish a putative link between strong synaptic currents and neuronal integrity. Thus far, the study of SuperAgers has led to the conclusion that these unique individuals carry with them a biological signature that now comprises a finding of larger, and healthier, ERC neurons relatively void of tau pathology. With time, it is likely that other factors that promote resistance and resilience to aging-related involutional phenomena will be discovered.

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Cognitive Aging Summits

2007– Cognitive Aging Summit I (Washington, DC)

The goals and objectives of the conference were to assess the status of current scientific knowledge in normal aging and changes in cognition associated with the aging process; explore new avenues of potential research within the scientific community that could lead to the development of pharmacological and behavioral interventions; and, ultimately, to improved outcomes for the aging; and raise the level of awareness both within the scientific community and among the public about the importance of this area of research and its tremendous value to society.

- **Lead to the Research Partnership in Cognitive Aging between the National Institute on Aging and the MBRF through the Foundation for the NIH in 2009**

2010—Cognitive Aging Summit II (Washington, DC)

Brought together 350 scientists from diverse disciplines to discuss critical questions in age-related brain and cognitive research and explore future avenues of research. The summit created tremendous excitement among researchers about building a more collaborative approach toward profiling brain health and cognitive function across the lifespan and developing healthy cognitive aging interventions. The concluding half-day segment of the Summit dealt with the development of clinical trials in which considerations for design and new opportunities were considered and discussed.

- **Produced the sentinel article published in The Journal of Gerontology titled "The other 87%" Authored by Drs. Wagster, King, Resnick and Raab**

2017—Cognitive Aging Summit III (Washington, DC)

The themes for Summit were cognitive and brain resilience and reserve. Over a day and a half, investigators from around the world delivered talks and discussed some of the most important issues facing the public as we seek to find ways to preserve or even improve cognitive function and brain health as we age.

Conference highlights:

The Summit agenda was organized around six topics centered on resilience and reserve, posed primarily in the form of questions:

1. How do we operationalize brain reserve, cognitive reserve, cognitive resilience, and compensation?
2. What are the threats to successful brain and cognitive aging?
3. What are the earlier life contributions to reserve and resilience?
4. What are the later life contributions to reserve, resilience and compensation?
5. How do we validate approaches that aim to harness reserve to improve the aging brain?
6. Innovative approaches in cognitive aging

In 2018, we plan to publish a set of scientific papers based on the content of each of the six sessions at the Summit as a special section in an issue of *Neurobiology of Aging*.

Cost of 2017 Summit: $197,008 (MBRF contributed $171,399 and NIA contributed $25, 610)

2024—Cognitive Aging IV (Bethesda, MD)

Plans are far along for Cognitive Aging Summit IV to be held in Bethesda, Maryland; March 20-21, 2024. Scientists from around the world will meet to continue the discussions and share research findings leading to further understanding in retarding and ameliorating age related cognitive decline and memory loss.

William G. Luttge Lectureship in Neuroscience*

2012—MBRF established a lectureship honoring the Founding Director of the Evelyn F. and William L. McKnight Brain Institute at the University of Florida

- Lectureship value--$250,000 (See Current Financial statement attached)
- Spendable Fund--$50,000 for immediate inauguration of the Lectureship
- Seventh lectureship was held on March 6, 2019
- Eighth lectureship scheduled for March 2020 was cancelled because of the Pandemic.
- Virtual Lectureship were held monthly throughout the Pandemic.
- Lectureship resumed on February 23, 2023, with Joshua A. Gordon, M.D., Ph.D., director of the National Institute of Mental Health, delivering the eighth annual William G. Luttge Lecture in Neuroscience delving into the roles of genetics, neural circuits and computational approaches in advancing new understanding and treatment of mental illnesses and cognitive Impairment Impact.

*Deceased, March 24, 2012

Dr. William G. Luttge Lectureship in Neuroscience

Financial Summary
January 1 to December 31, 2022

UNIVERSITY OF FLORIDA FOUNDATION ENDOWMENT ACCOUNT

06/01/2012 - Initial Donation	$	250,000
Additional contributions to the fund from various benefactors	$	350
Book Value as of 09/30/2022	$	250,350
**12/31/2022 Market Value projected	$	311,075
**12/31/2022 Return on Investment projected	$	45,934
**12/31/2022 Endowment Income to UF Side Spendable Projected	$	11,983

There are no outstanding matching funds.

Includes ***projected* amounts for the Fiscal Year 2023 second quarter (October 2022 - December 2022).
Fiscal Year 2023, Quarter 2 Financials have not been closed.

Endowment assets are invested through the University of Florida Investment Corporation (UFICO, created in 2004) to manage UF's investment portfolios. UFICO is headed by a Chief Investment Officer who reports to a volunteer Board of Directors and President of the University of Florida

UNIVERSITY OF FLORIDA SPENDABLE ACCOUNT

Dr. William G. Luttge Lectureship in Neuroscience

Beginning balance, January 1, 2022		$89,903
Endowment income transferred to the UF Side for Age Related Memory Loss Program		
January 2022	$2,996	
April 2022	$2,996	
July 2022	$2,995	
October 2022	$2,996	
Total endowment income transferred in to Spendable for the Age Related Memory Loss Program		$11,983
Expenditures		
Lecture Series Expenditures	$2,957	
Total Expenditures		$2,957
Ending balance December 31, 2022		$98,928

National Institute of Mental Health director delivers 2023 Luttge Lecture

PUBLISHED ON SOCIAL MEDIA, February 24, 2023

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By Michelle Jaffee

Joshua A. Gordon, M.D., Ph.D., director of the National Institute of Mental Health, delivered the eighth annual William G. Luttge Lecture in Neuroscience on Thursday, delving into the roles of genetics, neural circuits and computational approaches in advancing new understanding and treatment of mental illnesses.

Dr. Joshua A. Gordon

In a packed DeWeese Auditorium in the Evelyn F. and William L. McKnight Brain Institute of the University of Florida, an enthusiastic crowd of more than 150 neuroscience students and faculty members gathered for the first Luttge Lecture in four years, after a long interruption caused by the COVID-19 pandemic.

Gordon discussed efforts underway at NIMH, the lead federal agency for research on mental disorders and supporter of more than 3,000 research grants and contracts at universities, academic health centers and other research institutions. In describing opportunities and progress in the field, he highlighted studies including one he co-led with UF neuroscientist Nancy Padilla-Coreano, Ph.D., an assistant professor of neuroscience who studies how neural mechanisms may drive social behaviors.

Established and supported by the McKnight Brain Research Foundation, the William G. Luttge Lectureship honors late visionary neuroscientist William G. “Bill” Luttge, Ph.D., the founding director of UF’s Brain Institute that became the McKnight Brain Institute. The lecture is part of a joint seminar series of UF’s department of neuroscience and the McKnight Brain Institute and kicks off excitement for UF’s celebration of Brain Awareness Week, which this year will be held March 6-10.

Among the challenges for researchers, Gordon said, is that mental illness is the third highest form of disability in the U.S., after cardiovascular disease and cancer, and these illnesses often strike early in life and are for the most part chronic, causing morbidity and mortality through the lifespan.

In discussing opportunities for research, such as furthering understanding of how a genetic mutation may increase risk for schizophrenia, Gordon emphasized as next steps the importance of enriching the diversity of genetic data beyond people of European descent, a group disproportionately studied in this line of research in the past.

“On the whole, genetics represents an opportunity for understanding the neurobiology of schizophrenia,” he said.

Society for Neuroscience Annual Meeting

McKnight Brain Research Foundation and the McKnight Brain Institutes

Poster Reception

2008 – First Poster Reception was supported by the McKnight Brain Research Foundation and hosted by the Directors of the four McKnight Brain Institutes. Approximately 50 posters were summitted featuring research related to cognitive aging and age-related memory loss.

Posters are judged by Dr. Molly Wagster and Dr. Jon King from the National Institute on Aging. Cash awards are for top three posters - $500, $300 and $200 and $100 for each of three honorable mention awards. Vicki Hixon, from the MBI at UAB, is the volunteer coordinator of the Poster Reception program.

The 2020 Society for Neuroscience Annual Meeting was canceled due to the pandemic and no Poster Reception was held. There have been no poster receptions since 2019.

The Society for Neuroscience is scheduled to resume meeting again November 11 – 17, 2023, in Washington, DC. The Poster Reception hosted by the MBRF will resume the in-person poster reception in conjunction with the Society for Neuroscience meeting.

McKnight Brain Research Foundation
Clinical Translational Research Scholarship
in Cognitive Aging and Age-Related Memory Loss
and the McKnight Scholars and Mentors
July 2023

The McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss was established as a partnership with the American Brain Foundation in 2017. Ten McKnight Scholarships will be awarded for the period 2018 to 2022. The scholarships are funded by a $1.65 million grant from the McKnight Brain Research Foundation, through the American Brain Foundation (ABF) and the American Academy of Neurology (AAN).

This scholarship provides early career clinicians with $150,000 over two years in stipend and research-related costs. Applications for the award are open to young investigators interested in devoting significant research time in cognitive aging and age-related memory loss. The applications for the first two scholarships were submitted in 2017 and awards were made in spring of 2018.

The next application process will conclude on September 1, 2022. Review will take place in November of 2022 which will include three reviewers nominated by the McKnight Brain Research Foundation. Recipients will be notified in January 2023 and announcements made in early spring of 2023. It is hoped that the alumni scholars will present at the spring inter-institutional meeting of the MBIs in 2023.

2018 Scholars and Mentors (Alumni)
Brice McConnell, MD, PhD (Scholar – University of Colorado, Denver)
Benzi Kluger, MD, MS (Mentor – University of Colorado, Denver)

Kimberly Albert, PhD (Scholar – Vanderbilt)
Paul Newhouse, MD (Mentor – Vanderbilt)

2019 Scholars and Mentors (Current)
Christian Camargo, MD (Scholar – University of Miami)
Richard Wurtman, MD (Mentor)

Sanaz Sedaghat, PhD (Scholar – Northwestern)
Farzanch Sorond, MD, PhD (Mentor – Northwestern)

2020 Scholars and Mentors (Current)
Bryan Baxter, PhD (Scholar – Massachusetts General/Harvard)
Dara Manoach, PhD (Mentor – Massachusetts General/Harvard)

Sarah Getz, PhD (Scholar – University of Miami)
Bonnie Levin, PhD (Mentor – University of Miami)

2021 Scholars and Mentors (Current)
Wai-Ying Wendy Yau, MD (Scholar – Mass General Brigham)
Reisa Sperling, MD (Mentor – Mass General Brigham)

Reem Waziry, MBBCh, MPH, PhD (Scholar – Columbia University)
Daniel Belsky, PhD (Mentor – Columba University)

2022 Scholars and Mentors
Michael Kleiman, PhD (Scholar – UM Miller College of Medicine)
James E. Galvin, MD, MPH (Mentor – UM Miller College of Medicine)

Sarah Szymkowicz, PhD (Scholar – Vanderbilt)
Warren Taylor, MD, MHSc (Mentor – Vanderbilt)

2023 Scholars and Mentors
Eva Klinman, MD, PhD (Scholar – Washington University)
Andrew Yoo, PhD (Melntor – Washington University)

Sheena Baratono, MD, PhD (Scholar – Beth Israel Deaconess Harvard Medical Center)
Michael Fox, MD, PhD (Mentor – Harvard/Brigham and Women's Hospital)

McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss

Funded by the McKnight Brain Research Foundation through the American Brain Foundation and the American Academy of Neurology

Application Deadline: September 14, 2023

This award aims to support young investigators in clinical studies relevant to age-related cognitive decline and memory loss. The award also recognizes the importance of rigorous training in clinical research and encourages young investigators to seek opportunities to establish future careers in the area of human cognitive aging. **Please note: the focus should NOT be on a neurodegenerative dementia (e.g. Alzheimer's disease); however, proposals that focus on combined study of cognitive aging and neurodegenerative cognitive changes may be considered.**

The award will consist of a commitment of $65,000 per year for two years, plus a $10,000 per year stipend to support education and research-related costs for a total of $150,000. Supplementation of the award with other grants is permissible, but to be eligible to apply for this award, the other grant source(s) cannot exceed $75,000 annually.

The American Academy of Neurology is firmly committed to embracing the diversity among our members, applicants, and reviewers and affirms the importance of equity and inclusiveness within the AAN research program.

HOW TO APPLY

1. Visit AAN.com/view/ResearchProgram
2. Go to "2023 McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss"
3. Select "Apply now"

Please only submit one application - applicants are not allowed to submit applications for more than one award. Your application will also be considered for all relevant clinical research scholarship awards.

Visit the Frequently Asked Questions portion of the website for more information.

IMPORTANT DATES

September 14, 2023: Application deadline – Note that this is the deadline for all documents, including those from the mentor and chair. Applications will be declined if this information is not submitted by September 14.
January 2024: Notification of recipients
July 1, 2024: Funding begins

ELIGIBILITY

1. For the purpose of this scholarship, research is defined as patient-oriented research conducted with human participants, or translational research specifically designed to develop treatments or enhance identification of age-related cognitive decline and memory changes. These may include epidemiologic or behavioral studies, clinical trials, studies of disease mechanisms, the development of new technologies, and health outcomes research. Disease-related studies not directly involving humans are also encouraged if the primary goal is the development of therapies, diagnostic tests, or other tools to prevent or mitigate neurological diseases.
2. Recipient is interested in an academic career in neurological research who has completed residency or a PhD no more than 5 years prior to the beginning of this award (July 1, 2024). If you have completed both residency and a PhD, your eligibility is based on when you completed residency. If you completed a fellowship of any kind after residency, your eligibility is still based on the date you finished residency.
3. The proposed program of training and research must be performed entirely within an institution in the United States accredited by the relevant accrediting authority.
4. Research studies at the intersection of age-associated cognitive changes and disease-related cognitive impairment may be considered if a strong case can be made for their relevance to cognitive aging and age-related memory loss. However, research that is primarily focused on neurodegenerative diseases (e.g., Alzheimer's disease) will not be supported.

A successful application should include the following:

- Well-developed hypothesis: The hypothesis is testable and presented in clear language.
- Detailed statistical plan: Statistical methods are well-designed and detailed.
- Strong mentorship: There is clear demonstration of strong mentorship to support the project.
- Feasible primary outcomes: Each aim is feasible, focused, and logical.
- Innovation: Project concept is original, novel, and will advance the applicant's long-term career goals.
- Well-defined training plan: There is a clear and gap-based career development plan.

EVALUATION AND SELECTION

Applications are evaluated by reviewers based on the following criteria:

- Quality and originality of the research plan
- Applicant's ability and promise as a clinician-scientist based on prior record of achievement and career plan, and NIH Biosketch
- Quality and nature of the training to be provided and the mentor-specific, departmental, and institutional training environment
- Innovation of the research plan approach
- Project significance: the ability to progress the field or solve an important problem

REQUIRED ATTACHMENTS FOR APPLICATION

1. PDF of Three-page Research Plan, including brief statements of aims, background, contemplated approaches to methodology and any supporting preliminary data/figures. References do not count toward the page limit. The research plan should be written by the applicant and should represent their original work. However, the applicant is expected and encouraged to develop this plan based on discussion with the proposed mentor.
2. PDF of Applicant's NIH Biosketch. See this link for the most recent NIH Biosketch template

Once the above information is fully completed and **submitted** by the applicant:

3. The **chair** will receive an email with a link asking them to check a box confirming that the applicant's clinical service responsibilities will be restricted to no more than 30 percent of the applicant's time and include a list of applicant's non-research related service. The chair will NOT be asked to submit a letter.
4. The **mentor** will receive an email with a link to submit a letter of reference detailing their support of and commitment to the applicant's proposed research and training plan. The letter should be 1,000 words or less and specifically indicate the mentor's role in the development and preparation of the applicant's research plan including:
    - How the proposed research fits into the mentor's research program
    - Expertise and experience in the area of research proposed and the nature of the mentor's proposed time commitment to the applicant's supervision and training
    - Mentor's prior experience in the supervision, training, and successful mentoring of clinician scientists
    - Potential for applicant's future research career and comparison of applicant to other trainees
    - Institution's commitment to 70 percent protected research time
5. The **mentor** will also be required to upload a NIH Biosketch.

ANNUAL AND FINAL PROGRESS REPORTS

An annual progress report is due in May of the first year. Renewal of the award in year two is contingent upon presentation of a satisfactory progress report. Additionally, a final research report and a final expenditure report are due within 60 days following the close of the grant term. The final expenditure report must be prepared by the institution's financial office.

CONTACT INFORMATION:

Michelle Maxwell, Senior Manager, Research Program
Phone: (612) 928-6001
Email: mmaxwell@aan.com

To learn more about the Innovator Awards or to apply please go to:

https://mcknightbrain.org/innovator-awards-in-cognitive-aging/

https://www.afar.org/grants/mcknight-award.

McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss

The McKnight Brain Research Foundation (MBRF) and the American Federation for Aging Research (AFAR) will provide up to two 3-year awards of $750,000 (USD) each to advanced Assistant Professors and recently appointed Associate Professors (MDs and PhDs.) One award will be made to support studies focusing on clinical translational research and another award toward understanding basic biological mechanisms underlying cognitive aging and age-related memory loss.

The application deadline is July 31, 2023.

The Program

The major goal of the program is to identify emerging scientific leaders by building a cadre of outstanding research scientists across the United States to lead transformative research in the field of cognitive aging.

The program targets full-time independent investigators at the rank of Assistant Professor or Associate Professor (or equivalent) with established independent research programs who have already demonstrated a firm commitment to cognitive aging research. It will add substantial start-up support for a period of three years to help these investigators develop and/or expand an outstanding research program in cognitive aging and memory loss.

One award will be made to support innovative studies focusing on **clinical translational research** and another will support innovative studies of **basic biological mechanisms** underlying cognitive aging and age-related memory loss. It is expected that the proposed research will yield transformative discoveries and thus proposals are invited that are high risk/high gain in nature and that would be less suitable for conventional sources of funding. For example, this support could be deployed towards conducting a pilot clinical trial, developing proof-of concept interventions to ameliorate age associated cognitive impairment, gather preclinical data to accelerate testing of potential interventions, and further study the mechanistic basis of age-associated cognitive impairment in relevant experimental models with a view to identifying novel treatment targets. Scientists proposing to pursue basic research should clearly articulate the potential of their findings to be translated into clinically relevant strategies, and/or treatments. Research studies at the intersection of age-associated cognitive changes and disease-related cognitive impairment may be considered if a strong case can be made for their relevance to cognitive aging and age-related memory loss. However, research that is primarily focused on neurodegenerative diseases (e.g., Alzheimer's disease) will not be supported.

Two 3-year awards of $750,000 (USD) each will be made in 2023, of which a maximum of 10% may be used for indirect expenses or institutional overhead. To demonstrate a commitment to the investigator, the institution is asked to support the investigator's project through matching funds. The investigator needs to identify 50% in matching funds, which can only be from non-federal funds, and cannot be used by more than one project. This could be cash and/or in-kind matching, and can include faculty effort, and goods and services paid from departmental funds. For an in-kind match, the selection committee will determine whether this is equivalent to a monetary match.

Eligibility

To be eligible, the applicant must:

- Have completed research training prior to the beginning of this award (October 1, 2023):
  o PhD candidates: no more than 7 years from the completion of formal post-doctoral research training post-PhD,
  o MD or combined degree candidates: no more than 12 years from the date when finished residency.
- Be an independent investigator at the rank of Assistant Professor or Associate Professor (appointed no earlier than October 1, 2020), who has received R01 funding (or equivalent funding such as an NIH DP5, R35 or NSF Research awards.)
- Be tenure-track faculty or equivalent in an academic or non-profit institution with evidence of long-term institutional support as indicated by commitment of resources including independent laboratory space, start-up research funds and personnel. Candidates not in a tenure-track position are also eligible and should demonstrate similar evidence of long-term institutional support and not be in a time-limited appointment.
- Have a proven track record of research accomplishments in cognitive aging as indicated by their publications in high-impact journals, awards, and other metrics of peer recognition.
- Provide evidence of institutional matching funds as described in a **form completed by the Dean or Department Chair**.
- Be in full time employment at an academic or non-profit research institution in the United States.

The program **does not** provide support for:

- Senior faculty, i.e., at the rank of Associate Professor or higher who have held this position before October 1, 2020.
- Assistant Professors who have not yet received R01 or equivalent extramural independent funding.
- Investigators who are conducting research at a federal government or for-profit institution.
- See comment above about disease specific research.

Questions about eligibility and suitability of research project can be addressed to **grants@afar.org**.

Selection Criteria

Five criteria are used to determine the merit of an application:

- Qualifications of the applicant;
- Quality and promise of the proposed research and its relevance to cognitive aging/age-related memory loss;
- Novelty/impact of the proposed research and potential to have transformative clinical impact;
- Excellence of the research environment;
- The commitment by the institution to provide matching funds.

Application Procedures and Timeline

Please refer to the **application instructions**. Incomplete applications cannot be considered. All applications must be submitted via email to **afarapplication@afar.org**.

The applications will be reviewed by a committee whose recommendations will be presented to MBRF and AFAR for final funding decisions.

Please review **this link** which includes suggestions for submitting an LOI or application to AFAR. Click **here** for our Frequently Asked Questions page. If you are using animals in your research, please review **Principles of Animal Use for Gerontological Research** or this recent webinar recording from the Nathan Shock Centers of Excellence: **https://nathanshockcenters.org...**

MBRF and AFAR will not provide reviewer critiques to any applicants at any review level.

Timeline:
Application deadline: July 31, 2023

Anticipated Award Announcement: September 15, 2023

Award Start Date: October 1, 2023

Reporting Requirements

Investigators will be required to submit a brief **narrative report** annually on the progress of their research. Final narrative and financial reports are required within three months following the end date of the award.

Annual Meeting

Recipients of this award are expected to attend the AFAR Grantee Conference. The purpose of the meeting is to promote scientific and personal exchanges among recent AFAR grantees and experts in aging research. Grantees are also expected to attend the annual inter-institutional meeting of the MBRF.

Funder

McKNIGHT BRAIN RESEARCH FOUNDATION

Preserving memory, enhancing life

Founded in 1999 by Evelyn McKnight, the Foundation's specific goal is to better understand and alleviate age-related cognitive decline and memory loss. Cognitive changes due to the normal aging process may affect up to 87 percent of people age 65 and older, impacting abilities like processing speed and decision-making and contributing to some types of memory loss. The **McKnight Brain Research Foundation** works to champion research to better understand age-related cognitive decline and memory loss and educate the public on the steps that can be taken to maintain cognitive and brain health and age successfully.

In its first 20 years, the Foundation established Evelyn F. McKnight Brain Institutes at the University of Alabama at Birmingham, the University of Arizona, and the University of Miami, and the Evelyn F. and William L. McKnight Brain Institute at the University of Florida.

By partnering with the Foundation for the National Institutes of Health, and with the support of three Cognitive Aging Summits and the National Academy of Medicine Cognitive Aging Report, we have made great progress to better understand the effects of age-related cognitive decline and memory loss over the last two decades.

The McKnight Brain Research Foundation and the McKnight Brain Institutes are leaders in cognitive aging research. By providing research funding to promising investigators as they continue to embark upon independent careers, the MBRF proposes to build a core group of outstanding research scientists across the United States to lead transformative research in the field of cognitive aging.

The McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss

https://www.afar.org/grants/mcknight-award

2022 Recipients

Emilie Reas, PhD
Professor, University of California, San Diego
Project: *The mediating role of bloodbrain barrier dysfunction in effects of systemic inflammation on brain microstructure and memory*
Dr. Reas' lab uses advanced brain imaging methods to develop biomarkers of early Alzheimer's disease and to characterize the neurobiological changes leading to brain aging and dementia. Although inflammation and vascular dysfunction are risk factors for dementia, it remains unclear how they promote cognitive decline. Given the brain's privileged protection from the periphery by the "blood-brain barrier," the ways by which systemic inflammation affects the brain remains a critical unanswered question.

With support from the 2022 Innovator Award, Dr. Reas will examine relationships of blood-borne inflammatory factors with microstructural brain injury and memory, and to determine if a leaky blood-brain barrier mediates these associations. She will also evaluate whether individuals with high genetic risk for Alzheimer's disease show stronger connections between inflammation and brain microstructure, vascular leakage, and memory impairment. Findings are expected to clarify how inflammation and vascular dysfunction accelerate brain aging, and to guide development of therapeutic approaches to optimize cognitive health with age.

Tara Tracy, PhD
Assistant Professor, Buck Institute for Research on Aging
Project: *Role of KIBRA in Age-Related Memory Loss*
The dynamic modulation of the synaptic connections between neurons in the brain is critical for memory. Decline in synapse function underlies memory loss in aging, but little is known about what factors make synapses more vulnerable to dysfunction with age. KIBRA (KIdney/BRAin) is a postsynaptic protein required for synaptic plasticity and memory. Genetic variation in KIBRA is associated with age-related memory deficits in older adults. Given the critical role of KIBRA protein at synapses, the amount of KIBRA expressed in the brain may modulate susceptibility to memory decline in aging.

With funding from the 2022 Innovator Award, Dr. Tracy's lab will investigate how KIBRA levels impact synapse dysfunction and memory loss in aging. The goal of this research is to uncover mechanistic insight into the susceptibility of synapses to dysregulation in aging which could guide development of a therapeutic approach to repair synapse function as a treatment for age-related memory loss.

2021 Recipients

Lindsay De Biase, PhD
Assistant Professor, University of California, Los Angeles
Project: *Biological Age and Cognitive Resilience: with Special Emphasis on Ischemic Stroke Survivors*
Cognitive decline during aging is tightly linked to changes in the status of synapses, the connections between neurons where information is stored. Yet, the factors that regulate synapse health during aging are not well understood. Microglia are immune-like cells in the brain that respond to infection, disease, and injury. Surprisingly, these cells can also regulate the function and integrity of neuronal synapses.

With support from the Innovator Award in Cognitive Aging and Memory Loss, Dr. Biase will investigate the possibility that microglia shape synapse health during aging via modification of the extracellular matrix (ECM). The ECM is a meshwork of proteins and sugars woven tightly around neurons that potently regulates synapse stability. Recent studies and Dr. Biase's preliminary data show that microglia express numerous genes involved in building up and breaking down the ECM and that they can engulf ECM components. Dr. Biase will use multiple technical approaches to elucidate links between microglial-ECM interactions, synapse stability, and cognitive performance in aging mice and rats. The overarching goal is to identify molecular pathways for therapeutic modulation of microglial-ECM interactions to preserve cognition.

Saul Villeda, PhD
Assistant Professor, University of California, San Francisco
Project: *Caloric-restriction Induced Mechanisms of Cognitive Rejuvenation*
Identifying novel therapies to delay, and potentially reverse, age-related cognitive decline is critical given the projected increase of dementia-related disorders in an aging population. Caloric restriction counters age-related impairments in cognitive function in the aged brain. Dr. Villeda’s lab and others have shown that systemic interventions, including administration of blood plasma derived from young or exercised aged animals rejuvenates cognition at old age. The rejuvenating effects of caloric restriction mirror those observed with a youthful circulation, raising the possibility that caloric restriction similarly functions through blood factors to exert its beneficial effects.

With support from the Innovator Award in Cognitive Aging and Memory Loss, Dr. Villeda’s research will investigate the rejuvenating potential of caloric restriction-induced blood factors on the aged brain at the cellular, molecular and cognitive level. The proposed studies aim to identify molecular mechanisms that can be targeted to promote cognitive rejuvenation at old age, with clear therapeutic implications for dementia-related neurodegenerative disorders.

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July 2023

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Trustees' Secure Website

https://tmbrf.org/board-login

ID – mcknight

Password – X1234mcknight (only the X is capitalized)

McKnight Brain Research Foundation

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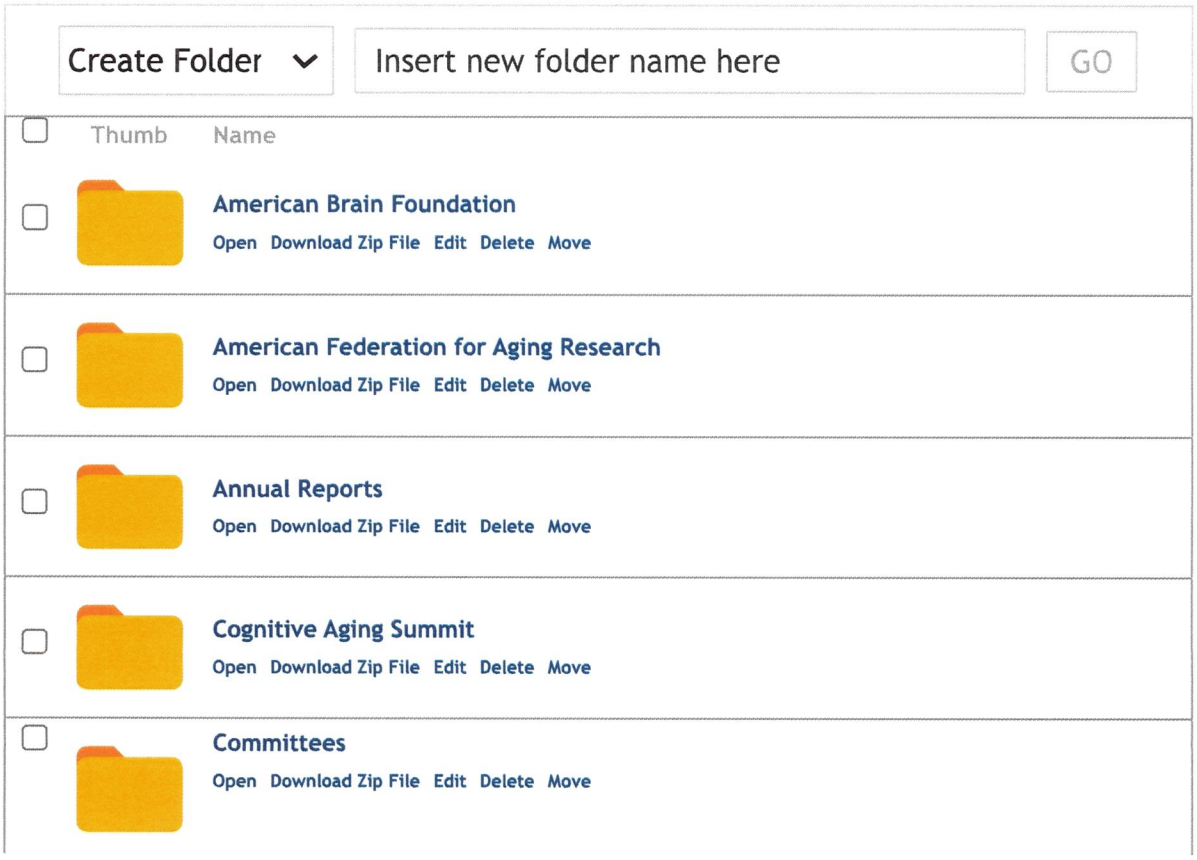

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